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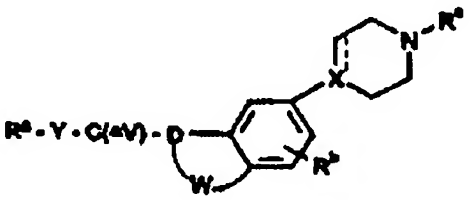
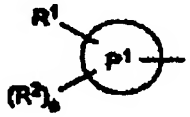
(54) **DERIVES INDOLIQUES A ACTIVITE DE RECEPTEUR ANTAGONISTE 5HT1A, 5HT1B, 5HT1D**

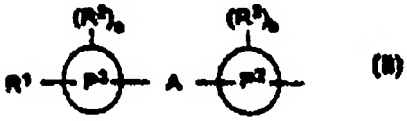
(54) **INDOLE DERIVATIVES HAVING COMBINED 5HT1A, 5HT1B AND 5HT1D RECEPTOR ANTAGONIST ACTIVITY**



(I)



(I)



(II)

(57) La présente invention concerne des composés représentés par la formule (I), leurs procédés de préparation, leur utilisation comme agents CNS, dans laquelle R^a est un groupe représenté par la formule (i) ou P^1 est un phényle, un aryle bicyclique, un noyau hétérocyclique de 5 à 7 chaînons contenant 1 à 3 hétéroatomes sélectionnés dans le groupe constitué

(57) Compounds of formula (I), processes for their preparation and their use as CNS agents are disclosed, in which R^a is a group of formula (i), in which P^1 is phenyl, bicyclic aryl, a 5- to 7-membered heterocyclic ring containing 1 to 3 heteroatoms selected from oxygen, nitrogen and sulphur, or a bicyclic heterocyclic ring containing 1 to 3 heteroatoms selected from oxygen,

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d'oxygène, d'azote et de soufre, or un noyau hétérocyclique bicyclique contenant 1 à 3 hétéroatomes sélectionnés dans le groupe constitué d'oxygène, d'azote et de soufre; R^1 et hydrogène, halogène, C_{1-6}alkyle, C_{3-6}cycloalkyle, COC_{1-6}alkyle, C_{1-6}alkoxy, hydroxy, hydroxyC_{1-6}alkyle, hydroxyC_{1-6}alcoxy, C_{1-6}alcoxyC_{1-6}alcoxy, C_{1-6}alkanoyl, nitro, trifluorométhyl, cyano, SR^9, SOR^9, SO_2R^9, $SO_2NR^{10}R^{11}$, CO_2R^{10}, $CONR^{10}R^{11}$, $CO_2NR^{10}R^{11}$, $CONR^{10}(CH_2)_cCO_2R^{11}$, $(CH_2)_cNR^{10}R^{11}$, $(CH_2)_cCONR^{10}R^{11}$, $(CH_2)_cNR^{10}COR^{11}$, $(CH_2)_cCO_2C_{1-6}$alkyl, $CO_2(CH_2)_cOR^{10}$, $NR^{10}R^{11}$, $NR^{10}CO_2R^{11}$, $NR^{10}CONR^{10}R^{11}$, CR^{10}=NOR^{11}, $NR^{10}COOR^{11}$, CNR^{10}=NOR^{11}, où R^{10} et R^{11} sont indépendamment hydrogen ou C_{1-6}alkyle et c est compris entre 1 et 4; R^2 est hydrogène, halogène, C_{1-6}alkyle, C_{3-6}cycloalkyle, C_{3-6}cycloalcényl, C_{1-6}alcoxy, acyle, aryle, acyloxy, hydroxy, nitro, trifluorométhyl, cyano, CO_2R^{10}, $CONR^{10}R^{11}$, $NR^{10}R^{11}$ où R^{10} et R^{11} sont tels que définis pour R^1; a est 1, 2 ou 3; ou R^a est un groupe représenté par la formule (ii), dans laquelle P^2 et P^3 sont indépendamment un phényl, un aryle bicyclique, un noyau hétérocyclique de 5 à 7 chaînons contenant 1 à 3 hétéroatomes sélectionnés dans le groupe constitué d'oxygène, d'azote et de soufre ou un groupe hétérocyclique bicyclique contenant 1 à 3 hétéroatomes sélectionnés dans le groupe constitué d'oxygène, d'azote ou de soufre; A est une liaison ou oxygène, $S(O)_m$ où m

nitrogen and sulphur; R^1 is hydrogen, halogen, C_{1-6}alkyl, C_{3-6}cycloalkyl, COC_{1-6}alkyl, C_{1-6}alkoxy, hydroxy, hydroxyC_{1-6}alkyl, hydroxyC_{1-6}alkoxy, C_{1-6}alkoxyC_{1-6}alkoxy, C_{1-6}alkanoyl, nitro, trifluoromethyl, cyano, SR^9, SOR^9, SO_2R^9, $SO_2NR^{10}R^{11}$, CO_2R^{10}, $CONR^{10}R^{11}$, $CO_2NR^{10}R^{11}$, $CONR^{10}(CH_2)_cCO_2R^{11}$, $(CH_2)_cNR^{10}R^{11}$, $(CH_2)_cCONR^{10}R^{11}$, $(CH_2)_cNR^{10}COR^{11}$, $(CH_2)_cCO_2C_{1-6}$alkyl, $CO_2(CH_2)_cOR^{10}$, $NR^{10}R^{11}$, $NR^{10}CO_2R^{11}$, $NR^{10}CONR^{10}R^{11}$, CR^{10}=NOR^{11}, $NR^{10}COOR^{11}$, CNR^{10}=NOR^{11}, where R^{10} and R^{11} are independently hydrogen or C_{1-6}alkyl and c is 1 to 4; R^2 is hydrogen, halogen, C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkenyl, C_{1-6}alkoxy, acyl, aryl, acyloxy, hydroxy, nitro, trifluoromethyl, cyano, CO_2R^{10}, $CONR^{10}R^{11}$, $NR^{10}R^{11}$ where R^{10} and R^{11} are as defined for R^1; a is 1, 2 or 3; or R^a is a group of formula (ii), wherein P^2 and P^3 are independently phenyl, bicyclic aryl, a 5- to 7-membered heterocyclic ring containing 1 to 3 heteroatoms selected from oxygen, nitrogen and sulphur, or a bicyclic heterocyclic group containing 1 to 3 heteroatoms selected from oxygen, nitrogen or sulphur; A is a bond or oxygen, $S(O)_m$ where m is 0 to 2, carbonyl, CH_2 or NR^4 where R^4 is hydrogen or C_{1-6}alkyl; R^1 is as defined above for formula (I) or R^1 is an optionally substituted 5 to 7-membered heterocyclic ring containing 1 to 3 heteroatoms selected

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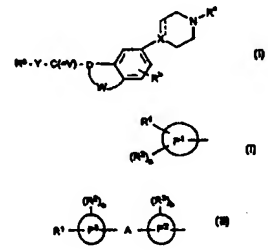
(54) Title: INDOLE DERIVATIVES HAVING COMBINED 5HT1A, 5HT1B AND 5HT1D RECEPTOR ANTAGONIST ACTIVITY



(57) Abstract

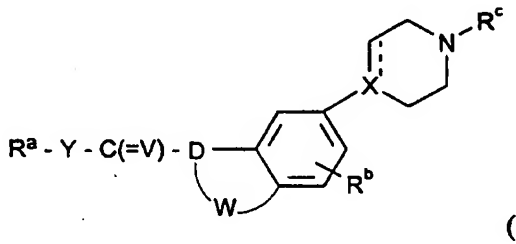
Compounds of formula (I), processes for their preparation and their use as CNS agents are disclosed, in which R^a is a group of formula (i), in which P^1 is phenyl, bicyclic aryl, a 5– to 7–membered heterocyclic ring containing 1 to 3 heteroatoms selected from oxygen, nitrogen and sulphur, or a bicyclic heterocyclic ring containing 1 to 3 heteroatoms selected from oxygen, nitrogen and sulphur; R^1 is hydrogen, halogen, C_{1-6}alkyl, C_{3-6}cycloalkyl, COC_{1-6}alkyl, C_{1-6}alkoxy, hydroxy, hydroxyC_{1-6}alkyl, hydroxyC_{1-6}alkoxy, C_{1-6}alkoxyC_{1-6}alkoxy, C_{1-6}alkanoyl, nitro, trifluoromethyl, cyano, SR^9, SOR^9, SO_2R^9, $SO_2NR^{10}R^{11}$, CO_2R^{10}, $CONR^{10}R^{11}$, $CO_2NR^{10}R^{11}$, $CONR^{10}(CH_2)_cCO_2R^{11}$, $(CH_2)_cNR^{10}R^{11}$, $(CH_2)_cCONR^{10}R^{11}$, $(CH_2)_cNR^{10}COR^{11}$, $(CH_2)_cCO_2C_{1-6}$alkyl, $CO_2(CH_2)_cOR^{10}$, $NR^{10}R^{11}$, $NR^{10}CO_2R^{11}$, $NR^{10}CONR^{10}R^{11}$, CR^{10}=NOR^{11}, $NR^{10}COOR^{11}$, CNR^{10}=NOR^{11}, where R^{10} and R^{11} are independently hydrogen or C_{1-6}alkyl and c is 1 to 4; R^2 is hydrogen, halogen, C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkenyl, C_{1-6}alkoxy, acyl, aryl, acyloxy, hydroxy, nitro, trifluoromethyl, cyano, CO_2R^{10}, $CONR^{10}R^{11}$, $NR^{10}R^{11}$ where R^{10} and R^{11} are as defined for R^1; a is 1, 2 or 3; or R^a is a group of formula (ii), wherein P^2 and P^3 are independently phenyl, bicyclic aryl, a 5– to 7–membered heterocyclic ring containing 1 to 3 heteroatoms selected from oxygen, nitrogen and sulphur, or a bicyclic heterocyclic group containing 1 to 3 heteroatoms selected from oxygen, nitrogen or sulphur; A is a bond or oxygen, $S(O)_m$ where m is 0 to 2, carbonyl, CH_2 or NR^4 where R^4 is hydrogen or C_{1-6}alkyl; R^1 is as defined above for formula (I) or R^1 is an optionally substituted 5 to 7–membered heterocyclic ring containing 1 to 3 heteroatoms selected from oxygen, nitrogen or sulphur; R^2 and R^3 are independently hydrogen, halogen, C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkenyl, C_{1-6}alkoxy, acyl, aryl, acyloxy, hydroxy, nitro, trifluoromethyl, cyano, CO_2R^{10}, $CONR^{10}R^{11}$, $NR^{10}R^{11}$ where R^{10} and R^{11} are as defined for R^1; and a and b are independently 1, 2 or 3; Y is –NH–, NR^5 where R^5 is C_{1-6}alkyl, or Y is $–CH_2–$ or –O–; V is oxygen or sulphur; D is nitrogen, carbon or a CH group; W is $(CR^{16}R^{17})_t$ where t is 2, 3 or 4 and R^{16} and R^{17} are independently hydrogen or C_{1-6}alkyl or W is $(CR^{16}R^{17})_u$–J where u is 0, 1, 2 or 3 and J is oxygen, sulphur, CR^{16}=CR^{17}, CR^{16}=N, =CR^{16}O, =CR^{16}S or =CR^{16}–NR^{17}; X is nitrogen or carbon; R^b is hydrogen, halogen, hydroxy, C_{1-6}alkyl, trifluoromethyl, C_{1-6}alkoxy, C_{2-6}alkenyl, C_{3-7}cycloalkyl optionally substituted by C_{1-4}alkyl, or aryl; R^c is hydrogen or C_{1-6}alkyl; and ..... is a single bond when X is nitrogen or a single or double bond when X is carbon.

INDOLE DERIVATIVES HAVING COMBINED 5HT1A, 5HT1B AND 5HT1D RECEPTOR ANTAGONIST ACTIVITY

The present invention relates to novel piperazine derivatives, processes for their preparation, and pharmaceutical compositions containing them.

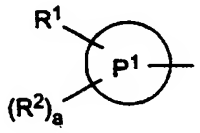
WO 95/06637, WO 95/06044 and WO 95/04729 disclose a series of piperazine derivatives which are said to possess $5HT_{1D}$ receptor antagonist activity. These compounds are alleged to be of use in the treatment of various CNS disorders such as depression. EPA 0533266/7/8 disclose a series of benzanilide derivatives which are said to possess 5-HT_{1D} receptor antagonist activity.

A structurally distinct class of compounds have now been found to exhibit combined $5HT_{1A}$, $5HT_{1B}$ and $5HT_{1D}$ receptor antagonist activity. It is expected that such compounds will be useful for the treatment and prophylaxis of various CNS disorders with the advantage of a relatively fast onset of action. In a first aspect, the present invention therefore provides a compound of formula (I) or a salt thereof:



(I)

in which R^a is a group of formula (i)



(i)

in which P^1 is phenyl, bicyclic aryl, a 5 to 7 membered heterocyclic ring containing 1 to 3 heteroatoms selected from oxygen, nitrogen and sulphur, or a bicyclic heterocyclic ring containing 1 to 3 heteroatoms selected from oxygen, nitrogen and sulphur;

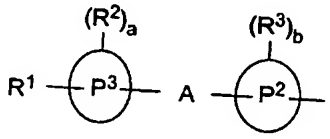
R^1 is hydrogen, halogen, C_{1-6}alkyl, C_{3-6}cycloalkyl, COC_{1-6}alkyl, C_{1-6}alkoxy, hydroxy, hydroxyC_{1-6}alkyl, hydroxyC_{1-6}alkoxy, C_{1-6}alkoxyC_{1-6}alkoxy, C_{1-6}alkanoyl, nitro, trifluoromethyl, cyano, SR^9, SOR^9, SO_2R^9, $SO_2NR^{10}R^{11}$, CO_2R^{10},

$CONR^{10}R^{11}$, $CO_2NR^{10}R^{11}$, $CONR^{10}(CH_2)_cCO_2R^{11}$, $(CH_2)_cNR^{10}R^{11}$, $(CH_2)_cCONR^{10}R^{11}$, $(CH_2)_cNR^{10}COR^{11}$, $(CH_2)_cCO_2C_{1-6}$alkyl, $CO_2(CH_2)_cOR^{10}$, $NR^{10}R^{11}$, $NR^{10}CO_2R^{11}$, $NR^{10}CONR^{10}R^{11}$, $CR^{10}=NOR^{11}$, $NR^{10}COOR^{11}$, $CNR^{10}=NOR^{11}$, where R^9, R^{10} and R^{11} are independently hydrogen or C_{1-6}alkyl and c is 1 to 4;

R^2 is hydrogen, halogen, C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkenyl, C_{1-6}alkoxy, C_{1-6}alkanoyl, aryl, acyloxy, hydroxy, nitro, trifluoromethyl, cyano, CO_2R^{10}, $CONR^{10}R^{11}$, $NR^{10}R^{11}$ where R^{10} and R^{11} are as defined for R^1;

a is 1, 2 or 3;

or R^a is a group of formula (ii)



(ii)

wherein P^2 and P^3 are independently phenyl, bicyclic aryl, a 5- to 7- membered heterocyclic ring containing 1 to 3 heteroatoms selected from oxygen, nitrogen and sulphur, or a bicyclic heterocyclic group containing 1 to 3 heteroatoms selected from oxygen, nitrogen or sulphur;

A is a bond or oxygen, $S(O)_m$ where m is 0 to 2, carbonyl, CH_2 , $-CH_2-CH_2-$, or NR^4 where R^4 is hydrogen or C_{1-6}alkyl;

R^1 is as defined above for formula (i) or R^1 is a 5 to 7-membered heterocyclic ring, containing 1 to 3 heteroatoms selected from oxygen, nitrogen or sulphur, optionally substituted by C_{1-6} alkyl, halogen or C_{1-6} alkanoyl;

R^2 and R^3 are independently hydrogen, halogen, C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkenyl, C_{1-6}alkoxy, C_{1-6}alkanoyl, aryl, acyloxy, hydroxy, nitro, trifluoromethyl, cyano, CO_2R^{10}, $CONR^{10}R^{11}$, $NR^{10}R^{11}$ where R^{10} and R^{11} are as defined for R^1;

and a and b are independently 0, 1, 2 or 3;

Y is -NH-, $-NR^5-$ where R^5 is C_{1-6}alkyl, or Y is $-CH_2-$ or -O-;

V is oxygen or sulphur;

D is nitrogen, carbon or a CH group; W is $(CR^{16}R^{17})_t$ where t is 2, 3 or 4 and R^{16} and R^{17} are independently hydrogen or C_{1-6}alkyl or W is $(CR^{16}R^{17})_u$-J where u is 0, 1, 2 or 3 and J is oxygen, sulphur, $CR^{16}=CR^{17}$, $CR^{16}=N$, $=CR^{16}O$, $=CR^{16}S$ or $=CR^{16}-NR^{17}$;
X is nitrogen or carbon;
R^b is hydrogen, halogen, hydroxy, C_{1-6}alkyl, trifluoromethyl, C_{1-6}alkoxy, C_{2-6}alkenyl, C_{3-7}cycloalkyl optionally substituted by C_{1-4}alkyl, or aryl;
R^c is hydrogen or C_{1-6}alkyl; and
— is a single bond when X is nitrogen or a single or double bond when X is carbon.

C_{1-6}alkyl groups whether alone or as part of another group may be straight chain or branched. The term 'acyloxy' is used herein to describe a group $-OC(O)C_{1-6}$alkyl. The term 'aryl' is used herein to describe, unless otherwise stated, a group such as phenyl. The term 'aralkyl' is used herein to describe, unless otherwise stated, a group such as benzyl.

The bicyclic aryl group represented by P^1, P^2 and/or P^3, which may be partially saturated, is preferably naphthyl.

Examples of bicyclic heterocyclic rings containing 1 to 3 heteroatoms selected from oxygen, nitrogen and sulphur include isoquinoline, indole, benzofuran, benzothiophene and preferably quinoline.

Examples of 5 to 7 membered heterocyclic rings containing 1 to 3 heteroatoms selected from oxygen, nitrogen and sulphur represented by P^1, P^2 and/or P^3, include thienyl, furyl, pyrrolyl, triazolyl, imidazolyl, oxazolyl, thiazolyl, oxadiazolyl, isothiazolyl, isoxazolyl, thiadiazolyl, pyrimidyl, pyridazinyl and pyrazinyl, and preferably pyridyl.

The heterocyclic rings as described above can be linked to the remainder of the molecule via a carbon atom or, when present, a suitable nitrogen atom. Such rings can also be saturated or partially saturated. Examples of saturated or partially saturated 5 to 7 membered heterocyclic rings include piperidine, pyrrolidine and morpholine. Examples of partially saturated bicyclic heterocyclic rings include dihydrobenzofuran, dihydrobenzothiophene, tetrahydroquinioline and tetrahydroisoquinoline

R^1 is preferably a halogen atom for example, fluorine, chlorine or bromine, and R^2 and/or R^3 are each preferably hydrogen, halogen for example a chloro group, or a C_{1-6}alkyl group for example a methyl group. When R^1 is 5 to 7-membered heterocyclic rings suitable optional substituents include C_{1-6} alkyl, C_{1-6} alkanoyl and halogen.

a and b are each preferably 1 or 2.

A is preferably a bond or oxygen, most preferably a bond.

Y is preferably -NH-.

V is preferably oxygen.

D is preferably nitrogen and the group W is preferably a $(CR^{16}R^{17})_t$ group where R^{16} and R^{17} are each advantageously hydrogen and t is suitably 2.

R^b is preferably hydrogen or a halogen atom for example chlorine, a C_{1-6}alkoxy group for example methoxy or a C_{1-6}alkyl group such as methyl or ethyl.

X is preferably nitrogen.

R^c is preferably a C_{1-6}alkyl group for example methyl.

Particularly preferred compounds according to the invention include:-

1-[(4-bromo-3-methylphenyl)aminocarbonyl]-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole,

1-[(4-bromo-3-methylphenyl)aminocarbonyl]-2,3-dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole,

1-[(2,3-dichlorophenyl)aminocarbonyl]-2,3-dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole,

2,3-Dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole,

2,3-Dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1-[5-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole,

1-[2,3-Dichloro-4-(pyridin-4-yl)phenylaminocarbonyl]-2,3-dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole,

2,3-Dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1-(quinolin-5-ylaminocarbonyl)-1H-indole,

2,3-Dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole,

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)phenylaminocarbonyl]-1H-indole,

5-Bromo-1-[3-chloro-4-(pyridin-4-yl)phenylaminocarbonyl]-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole,

2,3-Dihydro-5-methyl-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole,

1-[3-Chloro-4-(pyridin-4-yl)phenylaminocarbonyl]-2,3-dihydro-5-methyl-6-(4-methylpiperazin-1-yl)-1H-indole,

2,3-Dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-5-vinyl-1H-indole,

2,3-Dihydro-5-ethyl-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole,

1-[3-Chloro-4-(pyridin-4-yl)phenylaminocarbonyl]-2,3-dihydro-5-ethyl-6-(4-methylpiperazin-1-yl)-1H-indole,

2,3-Dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-5-trifluoromethyl-1H-indole,

1-[3-Chloro-4-(pyridin-4-yl)phenylaminocarbonyl]-2,3-dihydro-6-(4-methylpiperazin-1-yl)-5-trifluoromethyl-1H-indole,

2,3-Dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylacetyl]-1H-indole,

2,3-Dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1-[5-(pyridin-4-yl)-naphth-1-ylacetyl]-1H-indole,

2,3-Dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylacetyl]-1H-indole

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylacetyl]-1H-indole,

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylacetyl]-1H-indole,

2,3-Dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylacetyl]-5-vinyl-1H-indole,

5-Bromo-2,3-dihydro-6-(1-methylpiperidin-4-yl)-1-[4-(pyridin-4-yl)naphth-1-ylamino-carbonyl]-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[5-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole,

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[5-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole,

2,3-Dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1-(quinolin-6-ylaminocarbonyl)-1H-indole,

2,3-Dihydro-1-[4-(*t*-butoxycarbonylamino)phenylaminocarbonyl]-5-chloro-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-(quinolin-6-ylaminocarbonyl)-1H-indole,

6-Bromo-7-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1,2,3,4-tetrahydroquinoline,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-(4-phenoxyphenylaminocarbonyl)-1H-indole

5-Chloro-2,3-dihydro-1-[4-(4-chlorophenoxy)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-(quinolin-6-ylaminocarbonyl)-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-(3-phenoxyphenylaminocarbonyl)-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyrimidin-2-yl)phenylamino-carbonyl]-1H-indole,

1-(3-Benzoylphenylaminocarbonyl)-5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole,

1-(4-Benzoylphenylaminocarbonyl)-5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-(2-methylquinolin-6-ylaminocarbonyl)-1H-indole,

5-Chloro-2,3-dihydro-1-[4-(fur-2-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(thien-2-yl)phenylaminocarbonyl]-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[5-(pyridin-2-yl)naphth-1-ylacetyl]-1H-indole,

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[5-(pyridin-4-yl)naphth-1-ylacetyl]-1H-indole,

5-Chloro-2,3-dihydro-1-[4-(1-methylpiperidin-4-yl)naphth-1-ylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-1-[4-(2-methyloxazol-4-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(2-methylpyridin-4-yl)phenylamino-carbonyl]-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(2-methylpyridin-4-yl)phenylaminocarbonyl]-1H-indole,

5-Chloro-2,3-dihydro-1-[4-(2,6-dimethylpyridin-4-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Bromo-2,3-dihydro-1-[4-(2,6-dimethylpyridin-4-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

2,3-Dihydro-1-[4-(2,6-dimethylpyridin-4-yl)phenylaminocarbonyl]-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-1-[4-(2,6-dimethylpyridin-3-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Bromo-2,3-dihydro-1-[4-(2,6-dimethylpyridin-3-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

2,3-Dihydro-1-[4-(2,6-Dimethylpyridin-3-yl)phenylaminocarbonyl]-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(5-methyl-1,2,4-oxadiazol-3-yl)phenylaminocarbonyl]-1H-indole,

5-Chloro-2,3-dihydro-1-[4-(3-methyl-1,2,4-oxadiazol-5-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[3-(pyrimidin-2-yloxy)phenylaminocarbonyl]-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-{4-[N-methyl-N-(pyrimidin-2-yl)amino]phenylaminocarbonyl}-1H-indole,

5-Bromo-2,3-dihydro-1-[4-(fur-2-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(thien-3-yl)phenylaminocarbonyl]-1H-indole,

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(thiazol-2-yl)phenylaminocarbonyl]-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(thiazol-2-yl)phenylaminocarbonyl]-1H-indole,

1-[4-(5-Acetylthien-2-yl)phenylaminocarbonyl]-5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole,

1-(5-Bromonaphth-1-ylacetyl)-5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-(8-phenylquinolin-5-ylaminocarbonyl)-1H-indole,

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-(8-phenylquinolin-5-ylaminocarbonyl)-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[2-(2-phenylethyl)quinolin-6-ylaminocarbonyl]-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[5-(1-methylpiperidin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole,

5-Bromo-2,3-dihydro-1-[4-(isoquinolin-4-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-1-[4-(isoquinolin-4-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(quinolin-3-yl)phenylaminocarbonyl]-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(quinolin-3-yl)phenylaminocarbonyl)]-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[(2-methyl-1,2,3,4-tetrahydroisoquinolin-7-yl)aminocarbonyl]-1H-indole,

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[(2-methyl-1,2,3,4-tetrahydroisoquinolin-7-yl)aminocarbonyl]-1H-indole,

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(quinolin-8-yl)phenylaminocarbonyl]-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(quinolin-8-yl)phenylaminocarbonyl]-1H-indole,

5-Chloro-2,3-Dihydro-1-[4-(imidazol-1-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)phenylaminocarbonyl]-1H-indole,

2,3-Dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1-[(8-phenylquinolin-5-yl)aminocarbonyl]-1H-indole

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[(8-phenylquinolin-4-yl)aminocarbonyl]-1H-indole,

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[(8-phenylquinolin-4-yl)aminocarbonyl]-1H-indole,

2,3-Dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1-[(8-phenylquinolin-4-yl)aminocarbonyl]-1H-indole,

5-Chloro-2,3-dihydro-1-[4-(2,6-dimethyl-pyridin-4-yl)-3-methylphenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-1-[3-methyl-4-(6-methylpyridin-2-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Bromo-2,3-dihydro-1-[3-methyl-4-(6-methylpyridin-2-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

2,3-Dihydro-5-methoxy-1-[3-methyl-4-(6-methylpyridin-2-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-1-[5-(6-methylpyridin-2-yl)naphth-1-ylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

2,3-Dihydro-5-methoxy-1-[5-(6-methylpyridin-2-yl)naphth-1-ylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-6-(4-ethylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole,

5-Chloro-2,3-dihydro-6-(4-ethylpiperazin-1-yl)-1-[5-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole,

5-Chloro-2,3-dihydro-6-(piperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole hydrochloride,

5-Chloro-2,3-dihydro-6-(piperazin-1-yl)-1-[5-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole hydrochloride,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridazin-3-yl)phenylaminocarbonyl]-1H-indole,

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridazin-3-yl)phenylaminocarbonyl]-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyrazin-2-yl)phenylaminocarbonyl]-1H-indole,

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyrazin-2-yl)phenylaminocarbonyl]-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[(2-phenylpyridin-5-yl)aminocarbonyl]-1H-indole,

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[(2-phenylpyridin-5-yl)aminocarbonyl]-1H-indole,

5-Chloro-2,3-dihydro-1-[4-(6-methylpyridazin-3-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Bromo-2,3-dihydro-1-[4-(6-methylpyridazin-3-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-3-yl)phenylaminocarbonyl]-1H-indole,

5-Chloro-2,3-dihydro-1-[4-(5-methyloxazol-2-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

2,3-Dihydro-5-methoxy-1-[4-(5-methyloxazol-2-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Bromo-2,3-dihydro-1-[4-(5-methyloxazol-2-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-1-[4-(1-methylpyrazol-4-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Bromo-2,3-1-[4-(1-methylpyrazol-4-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-1-[4'-cyano-3'-methylbiphenyl-4-aminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Bromo-2,3-dihydro-1-[4'-cyano-3'-methylbiphenyl-4-aminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-1-[4-(2-methylpyridin-5-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Bromo-2,3-dihydro-1-[4-(2-methylpyridin-5-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-1-[5-(3-methyl-1,2,4-oxadiazol-5-yl)naphth-1-ylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

2,3-Dihydro-5-methoxy-1-[5-(3-methyl-1,2,4-oxadiazol-5-yl)naphth-1-ylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole.

5-Bromo-2,3-dihdyro-1-[5-(3-methyl-1,2,4-oxadiazol-5-yl)naphth-1-ylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-1-[5-(5-methyloxazol-2-yl)naphth-1-ylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

2,3-Dihydro-5-methoxy-1-[5-(5-methyloxazol-2-yl)naphth-1-ylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Bromo-2,3-dihydro-1-[3-methyl-4-(pyrimidin-2-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

2,3-Dihydro-5-methoxy-1-[3-methyl-4-(pyrimidin-2-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[3-methyl-4-(pyrimidin-2-yl)phenylaminocarbonyl]-1H-indole,

5-Bromo-2,3-dihydro-1-[3-methyl-4-(pyrimidin-5-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-1-[3-methyl-4-(pyrimidin-5-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

2,3-Dihydro-5-methoxy-1-[3-methyl-4-(pyrimidin-5-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Bromo-2,3-dihydro-1-[4-(2,6-dimethylpyridin-4-yl)-3-methylphenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

2,3-Dihydro-5-methoxy-1-[4-(2,6-dimethylpyridin-4-yl)-3-methylphenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-1-[5-(2,6-dimethylpyridin-4-yl)naphth-1-ylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Bromo-2,3-dihydro-1-[5-(2,6-dimethylpyridin-4-yl)naphth-1-ylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

2,3-Dihydro-1-[5-(2,6-dimethylpyridin-4-yl)naphth-1-ylaminocarbonyl]-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole

or pharmaceutically acceptable salts thereof.

Preferred salts of the compounds of formula (I) are pharmaceutically acceptable salts. These include acid addition salts such as hydrochlorides, hydrobromides, phosphates, acetates, fumarates, maleates, tartrates, citrates, oxalates, methanesulphonates and p-toluenesulphonates.

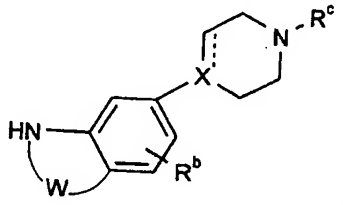
Certain compounds of formula (I) are capable of existing in stereoisomeric forms. It will be understood that the invention encompasses all geometric and optical isomers of the compounds of formula (I) and the mixtures thereof including racemates.

Compounds of the invention can be prepared using procedures known in the art. In a further aspect the present invention provides a process for the preparation of a compound of formula (I) or a pharmaceutically acceptable salt thereof which comprises:

(a) where D is nitrogen and Y is NH , coupling a compound of formula (II):

R^a -NC(=V) (II)

in which R^a and V are as defined in formula (I) or a protected derivative thereof with a compound of formula (III):



(III)

in which W, X, R^b and R^c are as defined in formula (I), or a protected derivative thereof; or

(b) where D is nitrogen and Y is NH or NR^5, reacting a compound of formula (IV)

R^a -NH_2 or R^a -NR^5H (IV)

in which R^a and R^5 are as defined in formula (I) with a compound of formula (III) together with an appropriate urea forming agent;

(c) where D is nitrogen, reacting a compound of formula (V)

$$R^a\text{-}Y\text{-}(C{=}O)\text{-}L^2 \quad (V)$$

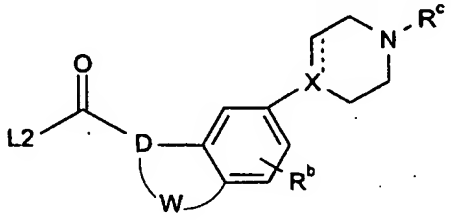
in which R^a is as defined in formula (I),

Y is $-CH_2-$ or -O- and L^2 is an appropriate leaving group, with a compound of formula (III);

d) where D is carbon or CH, reacting a compound of formula (VI)

$$R^a\text{-}NH_2 \quad (VI)$$

in which R^a is as defined in formula (I) with a compound of formula (VII)



(VII)

in which D is carbon or CH, W, X, R^b and R^c are as defined in formula (I) and L^2 is an appropriate leaving group

and optionally thereafter:

- removing any protecting groups,
- converting a compound of formula (I) into another compound of formula (I),
- forming a pharmaceutically acceptable salt.

The reaction in process (a) is conveniently effected in an organic solvent such as dichloromethane.

In process (b) the urea forming agent can be carbonyl diimidazole, triphosgene or phosgene, and carried out in an inert organic solvent such as dimethylformamide, tetrahydrofuran or dichloromethane at ambient or elevated temperature in the presence of a base such as triethylamine or pyridine.

In process (c) the leaving group L^2 may be a halogen e.g. chloro group and the reaction may be carried out in an inert organic solvent such as tetrahydrofuran or dichloromethane at ambient or elevated temperature in the presence of a base such as triethylamine or pyridine.

In process (d) the leaving group L^2 may be a halogen e.g. chloro group and the reaction may be carried out in an inert organic solvent such as tetrahydrofuran or dichloromethane at ambient or elevated temperature in the presence of a base such as triethylamine or pyridine.

Compounds of formula (I) can be converted into further compounds of formula (I) using standard techniques. For example, in the case wherein R^c is hydrogen, it is possible to introduce a C_{1-6}alkyl group by conventional alkylation using 1 molar equivalent of a C_{1-6}alkyl halide and 1 molar equivalent of a suitable base in an inert solvent.

Intermediate compounds of formula (II), (III), (IV) , (V) ,(VI) and (VII) can be prepared using standard procedures known in the art.

It will be appreciated to those skilled in the art that it may be necessary to protect certain reactive substituents during some of the above procedures. Standard protection and deprotection techniques can be used. For example, primary amines can be protected as phthalimide, benzyl, benzyloxycarbonyl or trityl derivatives. These groups can be removed by conventional procedures well known in the art.

Carboxylic acid groups can be protected as esters. Aldehyde or ketone groups can be protected as acetals, ketals, thioacetals or thioketals. Deprotection is achieved using standard conditions.

$5HT_{1A/1B/1D}$ receptor antagonists, and in particular the compounds of the present invention, are expected to be of use in the treatment of CNS disorders such as mood disorders, including depression, seasonal affective disorder and dysthymia; anxiety disorders, including generalised anxiety, panic disorder, agoraphobia, social phobia, obsessive compulsive disorder and post-traumatic stress disorder; memory disorders, including dementia, amnestic disorders and age-associated memory impairment; disorders of eating behaviours, including anorexia nervosa and bulimia nervosa and sleep disorders (including disturbances of Circadian rhythm). Other CNS disorders include motor disorders such as Parkinson's disease, dementia in Parkinson's disease, neuroleptic-induced Parkinsonism and tardive dyskinesias, as well as other psychiatric disorders.

$5HT_{1A/1B/1D}$ receptor antagonists, and in particular compounds of the present invention, may also be of use in the treatment of endocrine disorders such as hyperprolactinaemia, in the treatment of vasospasm (particularly in the cerebral vasculature) and hypertension, as well as disorders in the gastrointestinal tract where

changes in motility and secretion are involved. They may also be of use in the treatment of sexual dysfunction and hypothermia.

The present invention also provides a compound of general formula (I) or a physiologically acceptable salt or solvate thereof for use in the treatment of the aforementioned disorders.

In a further aspect the invention provides a method of treating the aforementioned disorders which comprises administering an effective amount to a patient in need of such treatment of a compound of general formula (I) or a pharmaceutically acceptable salt or solvate thereof.

In particular the invention provides a compound of general formula (I) or a physiologically acceptable salt or solvate thereof for use in the treatment or prophylaxis of depression.

It will be appreciated by those skilled in the art that the compounds according to the invention may advantageously be used in conjunction with one or more other therapeutic agents, for instance, different antidepressant agents.

The present invention also provides a pharmaceutical composition, which comprises a compound of formula (I) or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

A pharmaceutical composition of the invention, which may be prepared by admixture, suitably at ambient temperature and atmospheric pressure, is usually adapted for oral, parenteral or rectal administration and, as such, may be in the form of tablets, capsules, oral liquid preparations, powders, granules, lozenges, reconstitutable powders, injectable or infusible solutions or suspensions or suppositories. Orally administrable compositions are generally preferred.

Tablets and capsules for oral administration may be in unit dose form, and may contain conventional excipients, such as binding agents, fillers, tabletting lubricants, disintegrants and acceptable wetting agents. The tablets may be coated according to methods well known in normal pharmaceutical practice.

Oral liquid preparations may be in the form of, for example, aqueous or oily suspension, solutions, emulsions, syrups or elixirs, or may be in the form of a dry product for reconstitution with water or other suitable vehicle before use. Such liquid preparations may contain conventional additives such as suspending agents, emulsifying

agents, non-aqueous vehicles (which may include edible oils), preservatives, and, if desired, conventional flavourings or colorants.

For parenteral administration, fluid unit dosage forms are prepared utilising a compound of the invention or pharmaceutically acceptable salt thereof and a sterile vehicle. The compound, depending on the vehicle and concentration used, can be either suspended or dissolved in the vehicle. In preparing solutions, the compound can be dissolved for injection and filter sterilised before filling into a suitable vial or ampoule and sealing. Advantageously, adjuvants such as a local anaesthetic, preservatives and buffering agents are dissolved in the vehicle. To enhance the stability, the composition can be frozen after filling into the vial and the water removed under vacuum. Parenteral suspensions are prepared in substantially the same manner, except that the compound is suspended in the vehicle instead of being dissolved, and sterilisation cannot be accomplished by filtration. The compound can be sterilised by exposure to ethylene oxide before suspension in a sterile vehicle. Advantageously, a surfactant or wetting agent is included in the composition to facilitate uniform distribution of the compound.

The composition may contain from 0.1% to 99% by weight, preferably from 10 to 60% by weight, of the active material, depending on the method of administration.

The dose of the compound used in the treatment of the aforementioned disorders will vary in the usual way with the seriousness of the disorders, the weight of the sufferer, and other similar factors. However, as a general guide suitable unit doses may be 0.05 to 1000 mg, more suitably 1.0 to 200 mg, and such unit doses may be administered more than once a day, for example two or three a day. Such therapy may extend for a number of weeks or months.

The following Examples illustrate the preparation of compounds of the invention.

Description 1

4-Bromo-3-methylphenyl isocyanate

To a stirred suspension of 4-bromo-3-methylbenzoic acid (10.0g, 0.047 mole) in dichloromethane (300ml) was added oxalyl chloride (11.94g, 0.094 mole) followed by 3 drops of DMF. The mixture was stirred at room temperature for 60h, then the solution was concentrated *in vacuo* to afford the acid chloride as a red oil. This material was redissolved in dichloromethane (300ml) and cooled to 0°C. Tetrabutylammonium iodide (0.150g) was added, followed by a solution of sodium azide (4.36g, 0.066 mole) in water

(75ml) and the mixture was stirred vigorously at 0°C for 3h, then diluted with water (200ml) and the dichloromethane layer separated, dried (Na_2SO_4) and concentrated *in vacuo* (but not to complete dryness) to afford the acyl azide as a pale orange solid. This material was dissolved in toluene (300ml) and heated under reflux for 1h with stirring, then cooled and concentrated *in vacuo* to afford the title compound as a red brown oil (9.42g, 95%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 7.54 (d, 1H), 7.06 (d, 1H), 6.88 (dd, 1H), 2.46 (s, 3H).

Description 2

4-(Pyridin-4-yl)naphth-1-ylamine

A stirred suspension of 4-bromonaphth-1-ylamine (10g, 45 mmole) in 1,2-dimethoxyethane (400 ml) and water (100 ml) containing sodium carbonate (14g) was flushed with argon for 0.3h. Tetrakis(triphenylphosphine)palladium (0) (2.75g, 2.4 mmole) was added followed by 4-pyridylboronic acid (5.7g, 46 mmole) and the mixture heated at reflux for 5h. The mixture was concentrated *in vacuo* to a brown slurry and partitioned between dichloromethane and water. The aqueous was further extracted with dichloromethane and the combined organics dried (Na_2SO_4) and concentrated *in vacuo* to a brown solid (13.2g). Purification of the solid by flash chromatography eluting with ethyl acetate afforded the title compound as a yellow crystalline solid (7.8g, 78%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.68 (d, 2H), 7.90 (d, 2H), 7.30 (m, 5H), 6.84 (d, 1H), 4.32 (s, 2H)

Description 3

5-(Pyridin-4-yl)-1-naphthoic acid

The title compound was prepared from 5-bromo-1-naphthoic acid (EP 547442 A1) and 4-pyridylboronic acid using a similar procedure to Description 2.

^{1}H NMR (250 MHz, d^{6}DMSO) δ (ppm): 8.75 (d, 1H), 8.56 (dd, 2H), 7.98 (d, 1H), 7.78 (d, 1H), 7.56 (t, 1H), 7.45-7.34 (m, 4H)

Description 4

5-(Pyridin-4-yl)naphth-1-yl isocyanate

The title compound was prepared from 5-(pyridin-4-yl)-1-napthoic acid (D3) using a similar procedure to Description 1.

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.74 (d, 2H), 8.21 (d, 1H), 7.61-7.69 (m, 2H), 7.49-7.33 (m, 5H)

Description 5

4-(Pyridin-4-yl)aniline

The title compound was prepared from 4-bromoaniline and 4-pyridinylboronic acid using a similar procedure to Description 2 as a white solid (17%).

^{1}H NMR (250 MHz, d^6DMSO) δ (ppm): 8.68-8.63 (m, 2H), 7.78-7.68 (m, 4H), 6.84 (d, 2H), 5.94 (br s, 2H).

Description 6

3-Chloro-4-(pyridin-4-yl)aniline

3-Chloro-4-bromoacetanilide was reacted with 4-pyridinylboronic acid using a similar procedure to Description 2 to afford 3-chloro-4-(pyridin-4-yl)acetanilide. This material was hydrolysed by heating under reflux in a mixture of 2M NaOH solution and ethanol for 6h to afford the title compound as a pale yellow solid (5.5g, 73%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.65-8.58 (m, 2H), 7.38-7.33 (m, 2H), 7.13 (d, 1H), 6.80 (d, 1H), 6.64 (dd, 1H), 3.90 (br s, 2H).

Description 7

2,3-Dichloro-4-(pyridin-4-yl)aniline

The title compound was prepared from 4-bromo-2,3-dichloroacetanilide and 4-pyridinylboronic acid, followed by basic hydrolysis, using a similar procedure to the preparation of Description 6.

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.64 (d, 2H), 7.32 (d, 2H), 7.05 (d, 1H), 6.85 (d, 1H), 4.40 (br s, 2H).

Description 8

1-Acetyl-2,3-dihydro-6-nitro-1H-indole

A stirred solution of 2,3-dihydro-6-nitro-1H-indole (100g, 0.61 mole) in dichloromethane (1000 ml) at room temperature was treated dropwise over 20 min with acetic anhydride

(62 ml, 0.66 mole). The reaction mixture was stirred for a further 2h, then washed with 10% Na_2CO_3 solution (300 ml) dried (Na_2SO_4) and concentrated *in vacuo* to afford the title compound as a yellow solid (125g, 100%).

Description 9

1-Acetyl-6-amino-2,3-dihydro-1H-indole

A stirred suspension of 1-acetyl-2,3-dihydro-6-nitro-1H-indole (D8, 125g, 0.61 mole) in THF (5500 ml) was hydrogenated over 10% Pd-C (20g) at 50 psi for 20h. The catalyst was removed by filtration through a plug of kieselguhr and the filtrate concentrated *in vacuo* to afford the title compound as a beige solid (102g, 95%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 7.64 (d, 1H), 6.92 (d, 1H), 6.34 (dd, 1H), 4.01 (t, 2H), 3.82 (br s, 2H), 3.06 (t, 2H), 2.19 (s, 3H).

Description 10

1-Acetyl-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole

A stirred mixture of 1-acetyl-6-amino-2,3-dihydro-1H-indole (D9, 37.8g, 0.22 mole), mechlorethamine hydrochloride (46g, 0.24 mole) and anhydrous potassium carbonate (80g, 0.58 mole) in 1-butanol (1800 ml) was heated at reflux for 8h, then additional mechlorethamine hydrochloride (25g, 0.13 mole) and potassium carbonate (41g, 0.30 mole) were added and reflux continued for 3h. The reaction mixture was allowed to cool and then washed with water (1000 ml). The aqueous wash was extracted with ethyl acetate, and the extract combined with the 1-butanol solution and concentrated *in vacuo*. The brown oily residue (60g) was chromatographed on silica gel eluting with 0-8% MeOH/DCM to give an orange oil, which was trituated with ether to afford the title compound as a beige solid (12.2g, 22%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 7.98 (d, 1H), 7.04 (d, 1H), 6.59 (dd, 1H), 4.04 (t, 2H), 3.23-3.18 (m, 4H), 3.10 (t, 2H), 2.60-2.53 (m, 4H), 2.34 (s, 3H), 2.21 (s, 3H).

Description 11

2,3-Dihydro-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 1-acetyl-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D10) using a similar procedure to Description 13 as a beige solid (92%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 6.98 (dd, 1H), 6.34-6.27 (m, 2H), 3.53 (t, 2H), 3.32 (br s, 1H), 3.17-3.11 (m, 4H), 2.94 (t, 2H), 2.61-2.52 (m, 4H), 2.34 (s, 3H).

Description 12

1-Acetyl-5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole

A stirred solution of 1-acetyl-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D10, 1.1g, 0.0040 mole) in dichloromethane (100 ml) at -5°C under argon was treated dropwise over 15 min with a solution of N-chlorosuccinimide (0.73g, 0.0054 mole) in DCM (10 ml), then kept at -5°C for a further 0.5h and allowed to warm to room temperature over 1h. The reaction mixture was extracted with 2M HCl acid (60 ml) and the acid extract basified by addition of solid K_2CO_3 and extracted with DCM. The organic extract was dried (Na_2SO_4) and concentrated *in vacuo* to afford the title compound as a beige solid (1.45g, 100%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.05 (s, 1H), 7.15 (s, 1H), 4.06 (t, 2H), 3.20-3.05 (m, 4H), 3.12 (t, 2H), 2.70-2.55 (m, 4H), 2.37 (s, 3H), 2.22 (s, 3H).

Description 13

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole

A stirred solution of 1-acetyl-5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D12, 1.4g, 0.0048 mole) in 2M HCl acid (120 ml) was heated at reflux under argon for 5h. The reaction mixture was allowed to cool, basified by addition of solid K_2CO_3 and extracted with DCM. The extract was dried (Na_2SO_4) and concentrated *in vacuo* to afford the title compound as a beige solid (0.93g, 78%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 7.07 (s, 1H), 6.40 (s, 1H), 3.76 (br s, 1H), 3.56 (t, 2H), 3.01 (br s, 4H), 2.96 (t, 2H), 2.60 (br s, 4H), 2.35 (s, 3H).

Description 14

1-Acetyl-5-bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole

A stirred mixture of 1-acetyl-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D10, 2.0g, 0.0077 mole) and anhydrous potassium carbonate (2.12g, 0.015 mole) in a mixture of dichloromethane (100 ml) and methanol (50 ml) at -5°C under argon was treated portionwise over 20 min with benzyltrimethylammonium tribromide (3.14g, 0.0081 mole). The mixture was allowed to warm to room temperature over 1h, then concentrated

in vacuo and the residue dissolved in dichloromethane (150 ml), washed with water (2x100 ml), dried (Na_2SO_4) and concentrated *in vacuo* to afford the title compound as a beige solid (2.52g, 97%).

^1H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.06 (s, 1H), 7.34 (s, 1H), 4.06 (t, 2H), 3.13 (t, 2H), 3.07 (br s, 4H), 2.06 (br s, 4H), 2.35 (s, 3H), 2.21 (s, 3H).

Description 15

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole

A solution of 1-acetyl-2,3-dihydro-5-bromo-6-(4-methylpiperazin-1-yl)-1H-indole (D14, 0.60g, 1.8 mmole) in 2M hydrobromic acid (50 ml) was stirred at room temperature for 5 days, then basified by addition of solid K_2CO_3 and extracted with DCM. The extract was dried (Na_2SO_4) and concentrated *in vacuo* to afford the title compound as a brown solid (0.31g, 58%).

^1H NMR (250 MHz, $CDCl_3$) δ (ppm): 7.24 (s, 1H), 6.42 (s, 1H), 3.80 (br s, 1H), 3.56 (t, 2H), 3.01-2.92 (m, 6H), 2.59 (br s, 4H), 2.35 (s, 3H).

Description 16

1-Acetyl-2,3-dihydro-5-methyl-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 1-acetyl-2,3-dihydro-5-bromo-6-(4-methylpiperazin-1-yl)-1H-indole (D14) and tetramethyltin using a similar procedure to Description 18 as a beige solid (63%).

^1H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.0 (s, 1H), 6.98 (s, 1H), 4.02 (t, 2H), 3.11 (t, 2H), 2.97-2.92 (m, 4H), 2.56 (br s, 4H), 2.35 (s, 3H), 2.25 (s, 3H), 2.20 (s, 3H).

Description 17

2,3-Dihydro-5-methyl-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 1-acetyl-2,3-dihydro-5-methyl-6-(4-methylpiperazin-1-yl)-1H-indole (D16) using a similar procedure to Description 13 as a beige solid (89%).

^1H NMR (250 MHz, $CDCl_3$) δ (ppm): 6.94 (s, 1H), 6.44 (s, 1H), 3.52 (t, 2H), 2.95 (t, 2H), 2.92-2.86 (m, 4H), 2.55 (br s, 4H), 2.35 (s, 3H), 2.19 (s, 3H).

Description 18

1-Acetyl-2,3-dihydro-6-(4-methylpiperazin-1-yl)-5-vinyl-1H-indole

A stirred suspension of 1-acetyl-2,3-dihydro-5-bromo-6-(4-methylpiperazin-1-yl)-1H-indole (D14, 600 mg, 1.8 mmole) in dry DMF (15 ml) was treated with vinyltributyltin (0.78 ml, 2.7 mmole) and de-gassed by bubbling argon through for 20 min, then triethylamine (0.50 ml, 3.6 mmole) and tetrakis(triphenylphosphine)palladium(0) (200 mg) were added and the mixture was heated at 100°C under argon for 7 h. The reaction mixture was allowed to cool, diluted with EtOAc (150 ml), then extracted with 0.5M HCl acid (2 x 100 ml). The acid extract was basified by addition of solid K_2CO_3, then extracted with DCM (2 x 100 ml) and the extract dried (Na_2SO_4) and concentrated *in vacuo* to afford the title compound as a beige solid (480 mg, 95%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm):7.99 (s, 1H), 7.31 (s, 1H), 7.00 (dd, 1H), 5.58 (dd, 1H), 5.14 (dd, 1H), 4.05 (t, 2H), 3.14 (t, 2H), 3.02-2.94 (m, 4H), 2.57 (br s, 4H), 2.35 (s, 3H), 2.22 (s, 3H).

Description 19

2,3-Dihydro-6-(4-methylpiperazin-1-yl)-5-vinyl-1H-indole

A stirred solution of 1-acetyl-2,3-dihydro-6-(4-methylpiperazin-1-yl)-5-vinyl-1H-indole (D18, 250 mg, 9.0 mmole) in ethanol (25 ml) was treated with 10% NaOH solution (45 ml), de-gassed by bubbling argon through for 15 min, then heated under reflux for 7 h. The mixture was allowed to cool, concentrated *in vacuo* to approx. 40 ml volume and then extracted with DCM. The extract was dried (Na_2SO_4) and concentrated *in vacuo* to afford the title compound as a brown solid (170 mg, 80%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 7.30 (s, 1H), 6.98 (dd, 1H), 6.38 (s, 1H), 5.49 (dd, 1H), 5.01 (dd, 1H), 3.81 (br s, 1H), 3.56 (t, 2H), 2.99 (t, 2H), 2.96-2.90 (m, 4H), 2.56 (br s, 4H), 2.35 (s, 3H).

Description 20

1-Acetyl-2,3-dihydro-5-ethyl-6-(4-methylpiperazin-1-yl)-1H-indole

A stirred solution of 1-acetyl-2,3-dihydro-6-(4-methylpiperazin-1-yl)-5-vinyl-1H-indole (D18, 400 mg, 1.4 mmole) in ethanol (100 ml) was hydrogenated over 10% Pd-C (100 mg) at atmospheric pressure and temperature for 24 h. The catalyst was removed by filtration through kieselguhr and the filtrate concentrated *in vacuo* to afford the title compound as a beige solid (380 mg, 94%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.05 (s, 1H), 7.03 (s, 1H), 4.03 (t, 2H), 3.13 (t, 2H), 2.96-2.90 (m, 4H), 2.65 (q, 2H), 2.57 (br s, 4H), 2.35 (s, 3H), 2.20 (s, 3H), 1.21 (t, 3H).

Description 21

2,3-Dihydro-5-ethyl-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 1-acetyl-2,3-dihydro-5-ethyl-6-(4-methylpiperazin-1-yl)-1H-indole (D20) using a similar procedure to Description 13 as a beige solid (94%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 6.99 (s, 1H), 6.49 (s, 1H), 3.6 (br s, 1H), 3.53 (t, 2H), 2.97 (t, 2H), 2.90-2.83 (m, 4H), 2.59 (q, 2H), 2.54 (br s, 4H), 2.35 (s, 3H), 1.19 (t, 3H).

Description 22

1-Acetyl-2,3-dihydro-6-(4-methylpiperazin-1-yl)-5-trifluoromethyl-1H-indole

A stirred mixture of 1-acetyl-5-bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D14, 500 mg, 1.5 mmole), potassium trifluoroacetate (410 mg, 2.7 mmole) and copper (I) iodide (572 mg, 3.0 mmole) in dry DMF (16 ml) and toluene (10 ml) was heated at 130°C for 0.5 h under argon using a Dean and Stark head to trap toluene/water. The Dean and Stark head was replaced with a condenser and the mixture heated at 155°C for 34 h, then further potassium trifluoroacetate (410 mg) and copper (I) iodide (570 mg) were added and heating continued at 155°C for 3h. The reaction mixture was allowed to cool, then treated with dilute ammonia solution (200 ml) and DCM (150 ml), shaken well and then filtered through a plug of kieselguhr. The organic layer was separated, dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by chromatography on basic alumina eluting with ethyl acetate to afford the title compound as a beige solid (63%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.28 (s, 1H), 7.40 (s, 1H), 4.10 (t, 2H), 3.18 (t, 2H), 2.98-2.92 (m, 4H), 2.56 (br s, 4H), 2.35 (s, 3H), 2.24 (s, 3H).

Description 23

2,3-Dihydro-6-(4-methylpiperazin-1-yl)-5-trifluoromethyl-1H-indole

A solution of 1-acetyl-2,3-dihydro-6-(4-methylpiperazin-1-yl)-5-trifluoromethyl-1H-indole (D22, 260 mg, 1.1 mmole) in 2M HCl acid (25 ml) and ethanol (25 ml) was kept at room temperature for 7 days, then concentrated *in vacuo* to approx. 25 ml volume. The aqueous residue was basified with solid K_2CO_3, then extracted with DCM and the extract dried (Na_2SO_4) and concentrated *in vacuo* to afford the title compound as a beige solid (300 mg, 91%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 7.30 (s, 1H), 6.57 (s, 1H), 4.01 (br s, 1H), 3.63 (t, 2H), 3.01 (t, 2H), 2.92-2.85 (m, 4H), 2.54 (br s, 4H), 2.34 (s, 3H).

Description 24

4-(Pyridin-4-yl)naphth-1-ylacetic acid

4-Bromonaphth-1-ylacetic acid (1g, 3.78 mmole, J. Org. Chem., 1951, 16, 1588) in 1,2-dimethoxyethane (50 ml) was treated with pyridin-4-ylboronic acid (465 mg, 3.78 mmole), sodium hydrogen carbonate (952 mg, 11.3 mmole) and water (10 ml). A stream of argon was bubbled through the mixture for 15 min, then tetrakis (triphenylphosphine) palladium (0) (200 mg, 0.17 mmole) was added and the mixture heated under reflux for 18h. The mixture was then concentrated *in vacuo* to a gum, which was partitioned between 2M sodium hydroxide solution and dichloromethane. The aqueous layer was separated, adjusted to pH 7 by addition of aqueous potassium carbonate solution and extracted with dichloromethane. The dichloromethane extract was dried (Na_2SO_4) and concentrated *in vacuo* to give the title compound, which crystallised from ether as needles mp 210-215°C (465 mg, 46%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.55 (d, 2H), 8.0 (d, 1H), 7.7 (d, 1H), 7.5-7.3 (m, 5H), 7.2 (d, 1H), 6.1 (br s, 1H), 4.0 (s, 2H).

Description 25

5-(Pyridin-4-yl)napth-1-ylacetic acid

The title compound was prepared from 5-bromonaphth-1-ylacetic acid (Bull. Soc. Chim. Fr., 1968, 7, 2957) and pyridin-4-ylboronic acid using a similar procedure to Description 24.

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.72 (d, 2H), 8.13 (d, 1H), 7.76 (d, 1H), 7.60 (t, 1H), 7.40-7.50 (m, 3H), 7.44 (d, 2H), 4.12 (s, 2H).

Description 26

Quinolin-6-yl isocyanate

The title compound was prepared from 6-quinolinecarboxylic acid using a similar procedure to Description 1.

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.89 (dd, 1H), 8.13 - 8.06 (m, 2H), 7.52 (d, 1H), 7.48 - 7.41 (m, 2H).

Description 27

3-(4-Methylpiperazin-1-yl)-1-nitrobenzene

To a solution of 3-nitroaniline (15.0g, 0.11 mole) in 2-butanol (500ml) was added K_2CO_3 (52.5g, 0.385 mole) and mechlorethamine hydrochloride (31.4g, 0.16 mole). The mixture was refluxed under argon with stirring for 18h, then more mechlorethamine hydrochloride (17.5g, 0.09 mole) and K_2CO_3 (25.0g, 0.18 mole) were added and heating under reflux was continued for 24h. The 2-butanol was removed *in vacuo* and the residue partitioned between H_2O (300 ml) and CH_2Cl_2 (300ml). The CH_2Cl_2 was separated and the aqueous re-extracted with CH_2Cl_2 (3 x 200ml). The organics were combined, dried (Na_2SO_4) and concentrated *in vacuo* to afford an orange oil, which was purified by column chromatography on silica gel eluting with 0-4% MeOH/CH_2Cl_2. The title compound was an orange oil (16.72g, 70%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 7.72 (d, 1H), 7.65 (dd, 1H), 7.37 (t, 1H), 7.19 (dd, 1H), 3.31 (t, 4H), 2.59 (t, 4H), 2.37 (s, 3H).

Description 28

3-(4-Methylpiperazin-1-yl)aniline

3-(4-Methylpiperazin-1-yl)-1-nitrobenzene (D27, 8.10g, 0.037 mole) was dissolved in EtOH (250ml) and hydrogenated over 10% Pd/C (2g) at room temperature and pressure for 18h. The catalyst was filtered off and the filtrate concentrated *in vacuo* to afford the title compound as a pale yellow oil (6.64g, 95%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 7.04 (t, 1H), 6.37 (dd, 1H), 6.26 (d, 1H), 6.21 (dd, 1H), 3.60 (br s, 2H), 3.18 (t, 4H), 2.56 (t, 4H), 2.34 (s, 3H).

Description 29

7-(4-Methylpiperazin-1-yl)quinoline

3-(4-Methylpiperazin-1-yl)aniline (D28, 6.6g, 0.035mole) was covered with glycerol (8ml, 0.1 mole) and conc. H_2SO_4 acid (5.2ml, 0.097 mole) was carefully added dropwise, with stirring, over 10 min. An air condenser was fitted, iodine (100mg) added and the reaction heated with stirring at 100°C for 3h, then at 150°C for 4h. The reaction was cooled and poured into water (250ml). The aqueous was basified to pH10 with K_2CO_3 and extracted into CH_2Cl_2 (3 x 300ml). The organics were combined, dried (Na_2SO_4) and concentrated *in vacuo* to give a dark brown oil, which was purifed by column chromatography on basic alumina eluting with 2% MeOH/CH_2Cl_2. The title compound was a yellow solid (4.05g, 52%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.78 (m, 1H), 8.0 (dd, 1H), 7.67 (d, 1H), 7.37 (d, 1H), 7.33 (dd, 1H), 7.19 (dd, 1H), 3.40 (t, 4H), 2.63 (t, 4H), 2.38 (s, 3H).

Description 30

7-(4-Methylpiperazin-1-yl)-1,2,3,4-tetrahydroquinoline

7-(4-Methylpiperazin-1-yl)quinoline (D29, 3.71g, 0.016 mole) was dissolved in EtOH (100ml) and AcOH (5ml) and hydrogenated at 50psi and room temperature over 5% Pt/C (1.0g) for 84h. The catalyst was filtered off, the solvents removed *in vacuo* and the residue partitioned between 10% Na_2CO_3 (aq) and CH_2Cl_2. The CH_2Cl_2 was separated, dried (Na_2SO_4) and concentrated *in vacuo* to afford the title compound as a pale orange/brown solid (3.60g, 95%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 6.84 (d, 1H), 6.27 (dd, 1H), 6.05 (d, 1H), 3.5 (br s, 1H), 3.27 (t, 2H), 3.12 (t, 4H), 2.68 (t, 2H), 2.55 (t, 4H), 2.33 (s, 3H), 1.91 (quintet, 2H).

Description 31

7-(4-Methylpiperazin-1-yl)-1-trifluoroacetyl-1,2,3,4-tetrahydroquinoline

To a stirred solution of 7-(4-methylpiperazin-1-yl)-1,2,3,4-tetrahydroquinoline (D30, 1.0g, 4.3 mmole) in CH_2Cl_2 (30ml), cooled in ice, under argon, was added trifluoroacetic anhydride (0.67ml, 4.8 mmole) dropwise. After 30 min at 0°C the mixture was warmed to room temperature over 30 min, then washed with dilute $NaHCO_3$ (aq). The CH_2Cl_2 was separated, dried (Na_2SO_4) and concentrated *in vacuo* to afford the title compound as a viscous yellow oil (1.42g, 100%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 7.26 (d, 1H), 7.06 (d, 1H), 6.78 (dd, 1H), 3.81 (t, 2H), 3.25 (t, 4H), 2.72 (br s, 6H), 2.45 (s, 3H), 2.05 (quintet, 2H).

Description 32

6-Bromo-7-(4-methylpiperazin-1-yl)-1-trifluoroacetyl-1,2,3,4-tetrahydroquinoline

The title compound was prepared from 7-(4-methylpiperazin-1-yl)-1-trifluoroacetyl-1,2,3,4-tetrahydroquinoline (D31) using a similar procedure to Description 14.

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 7.39 (s, 1H), 7.26 (s, 1H), 3.82 (t, 2H), 3.29 (br s, 4H), 2.99 (br s, 4H), 2.82 (br s, 2H), 2.62 (s, 3H), 2.05 (quintet, 2H).

Description 33

6-Bromo-7-(4-methylpiperazin-1-yl)-1,2,3,4-tetrahydroquinoline

To a stirred solution of 6-bromo-7-(4-methylpiperazin-1-yl)-1-trifluoroacetyl-1,2,3,4-tetrahydroquinoline (D32, 0.74g, 1.8 mmole) in MeOH (30ml) was added K_2CO_3 (s) (0.50g, 3.6 mmole). After 18h at room temperature the MeOH was removed *in vacuo* and the residue partitioned between CH_2Cl_2 and 10% Na_2CO_3 (aq). The CH_2Cl_2 was separated, dried (Na_2SO_4) and concentrated *in vacuo* to afford the title compound as a yellow/brown solid (0.55g, 98%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 7.10 (s, 1H), 6.19 (s, 1H), 3.85 (br s, 1H), 3.26 (m, 2H), 2.99 (br s, 4H), 2.67 (t, 2H), 2.59 (br s, 4H), 2.35 (s, 3H), 1.89 (quintet, 2H).

Description 34

1-Butyryl-2,3-dihydro-6-nitro-1H-indole

2,3-Dihydro-6-nitro-1H-indole (16.4g, 100 mmole) in CH_2Cl_2 (200ml) was treated with butyryl chloride (10.6g, 100 mmole) and Et_3N (10.1g, 100 mmole) with continuous stirring at room temperature for 2h. The reaction was then washed successively with 5N HCl and saturated aqueous K_2CO_3 solution. The reaction was then dried (Na_2SO_4) and concentrated *in vacuo* to a gum which crystallised from petrol as needles to give the title compound (23.4g, 100%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 9.0 (s, 1H), 7.85 (dd, 1H), 7.25 (d, 1H), 4.15 (t, 2H), 3.3 (t, 2H), 2.4 (t, 2H), 1.8 (q, 2H), 1.0 (t, 3H).

Description 35

6-Amino-2,3-dihydro-1-butyryl-1-H-indole

1-Butyryl-2,3-Dihydro-6-nitro-1H-indole (D34, 19.8g, 84.4 mmole) was stirred with 10% palladium on charcoal (2g) in MeOH (200ml) under an atmosphere of hydrogen at 50psi at such a rate that the temperature rose to 60°C and the uptake of hydrogen ceased. The reaction was then filtered through celite and the celite washed with hot MeOH to ensure that no product was retained. The filtrate was evaporated *in vacuo* to give the title compound (13.3g, 77%) as needles.

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 7.5 (s, 1H), 6.85 (d, 1H), 6.2 (dd, 1H), 4.9 (s, 2H), 4.0 (t, 2H), 2.9 (t, 2H), 2.4 (t, 2H), 1.6 (q, 2H), 0.95 (t, 3H).

Description 36

1-Butyryl-2,3-dihydro-6-iodo-1H-indole

A stirred solution of 6-amino-1-butyryl-2,3-dihydro-1H-indole (D35, 3.0g, 0.015mole) in a mixture of conc. H_2SO_4 (3ml) and water (35ml) at 0°C was treated dropwise (tip of the addition funnel touching the liquid surface) with a solution of sodium nitrite (1.1g, 0.016mole) in water (10ml) whilst maintaining the temperature below 5°C. This mixture was then stirred for a further 20 min at <3°C before adding it dropwise to a solution of potassium iodide (2.66g, 0.016mole) in water (10ml) at 0°C. Slight effervescence was seen and a dark orange suspension formed. The mixture was stirred for a further 1.5h while allowing to warm to room temperature. The product was extracted with EtOAc (3x), the organics washed ($Na_2S_2O_3$ solution) and dried (Na_2SO_4) to give, on evaporation, the title compound as an orange solid (3.3g, 70%).

^{1}H NMR (250 MHz,$CDCl_3$) δ(ppm): 8.64 (s, 1H), 7.32 (dd, 1H), 6.90 (d, 1H), 4.04 (t, 2H), 3.13 (t, 2H), 2.39 (t, 2H), 1.75 (m, 2H), 1.02 (t, 3H).

Description 37

1-Butyryl-2,3-dihydro-6-(pyridin-4-yl)-1H-indole

A suspension of 1-butyryl-2,3-dihydro-6-iodo-1H-indole (D36, 3.28g, 10.4mmole) in dimethoxyethane (120ml) and water (30ml) containing Na_2CO_3 (3.85g, 36.4mmole) was flushed with argon for 1h. To the mixture was added 4-pyridylboronic acid (1.3g, 10.8mmole) and tetrakis(triphenylphosphine)palladium(0) (600mg, 0.52mmole) and the mixture heated at reflux for 1h. The mixture was allowed to cool, evaporated *in vacuo* and the residue partitioned between water and CH_2Cl_2. The aqueous was extracted further with CH_2Cl_2 (2x), the organics combined and dried (Na_2SO_4) to give on evaporation a

dark brown oil, which was purified by flash chromatography (eluant 5% MeOH/CH_2Cl_2) to give the title compound as a brown solid (1.5g, 54%).

^1H NMR (250 MHz,$CDCl_3$) δ(ppm): 8.61 (m, 3H), 7.53 (d, 2H), 7.29 (m, 2H), 4.13 (t, 2H), 3.25 (t, 2H), 2.44 (t, 2H), 1.79 (m, 2H), 1.04 (t, 3H).

Description 38

1-Butyryl-2,3-dihydro-6-(1-methylpiperidin-4-yl)-H-indole

To a solution of 1-butyryl-2,3-dihydro-6-(pyridin-4-yl)-1H-indole (D37, 1.5g, 5.63mmole) in acetone (50ml) was added iodomethane (1.6g, 11.3mmole) and the mixture left to stand overnight. Filtration gave an orange solid (1.2g) which was dissolved in ethanol (25ml) and water (25ml) and the solution cooled to 0°C. To the solution was added sodium borohydride (166mg, 4.4mmole) portionwise over 5 min. and the mixture stirred for a further 10 min. To the mixture was added 2M NaOH solution (16ml) and water (40ml) and the product extracted with CH_2Cl_2 (2x), dried (Na_2SO_4) and evaporated *in vacuo* to a brown oil (1.0g). The oil was then dissolved in ethanol (50ml) and hydrogenated over 10% Pd-C (100mg) at 50 psi and 50°C for 72h. Filtration and evaporation of the filtrate *in vacuo* gave the title compound as a white solid (710mg, 44%).

^1H NMR (250 MHz,$CDCl_3$) δ(ppm): 8.19 (s, 1H), 7.11 (d, 1H), 6.88 (d, 1H), 4.04 (t, 2H), 3.15 (t, 2H), 2.96 (br d, 2H), 2.48 (m, 1H), 2.39 (t, 2H), 2.31 (s, 3H), 2.03 (m, 2H), 1.82 (m, 6H), 1.02 (t, 3H).

Description 39

5-Bromo-2,3-dihydro-6-(1-methylpiperidin-4-yl)-1H-indole

To a stirred solution of 1-butyryl-2,3-dihydro-6-(1-methylpiperidin-4-yl)-1H-indole (D38, 2.32mmole) in acetic acid (20ml) was added N-bromosuccinimide(454mg, 2.55mmole) and the mixture stirred at room temperature overnight. The mixture was diluted with water and basified with solid K_2CO_3. Extraction with CH_2Cl_2, drying (Na_2SO_4) of the organics and evaporation *in vacuo* gave an off-white solid (890mg). A portion of the solid (790mg, 2.16mmole) in ethanol (20ml) and 2M NaOH solution (30ml) was heated at 80°C under argon for 72h. The product was extracted with CH_2Cl_2, the organics dried (Na_2SO_4) and evaporated *in vacuo* to give the title compound as an orange solid (647mg, 100%).

^{1}H NMR (250 MHz,$CDCl_3$) δ(ppm): 7.24 (s, 1H), 6.57 (s, 1H), 3.55 (t, 2H), 2.99 (m, 4H), 2.88 (m, 1H), 2.33 (s, 3H), 2.10 (m, 2H), 1.75 (m, 4H). NH not observed

Description 40

4-(*t*-Butoxycarbonylamino)aniline

To a stirred solution of phenylenediamine (2.0g, 18.5mmole) in CH_2Cl_2 (50ml) at 0°C was added di-*tert*-butyl dicarbonate (4.25ml, 18.5mmole) and the mixture stirred whilst warming to room temperature for 16h. Evaporation *in vacuo* gave the title compound in 80% purity, with the di-Boc compound making up the remainder (3.79g, 98%).

^{1}H NMR (of title compound) (250 MHz,$CDCl_3$) δ(ppm): 7.13 (d, 2H), 6.63 (d, 2H), 6.27 (br s, 1H), 3.50 (br s, 2H), 1.50 (s, 9H).

Description 41

4-(Pyrimidin-2-yl)benzoic acid

The title compound was prepared from 4-carboxyphenylboronic acid and 2-bromopyrimidine in a similar manner to Description 2, obtained as a pale buff powder (35%).

^{1}H NMR (250 MHz, d^6DMSO) δ (ppm): 12.95 (s, 1H), 8.87 (d, 2H), 8.41 (d, 2H), 8.00 (d, 2H), 7.41 (t, 1H).

Description 42

4-(Pyrimidin-2-yl)phenyl isocyanate

The title compound was prepared from 4-(pyrimidin-2-yl)benzoic acid (D41) in a similar manner to Description 1, obtained as a pale yellow powder (83%).

(^{1}H NMR - not recorded due to insolubility in $CDCl_3$).

Description 43

5-Chloro-2,3-dihydro-1-(4-iodophenylaminocarbonyl)-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) and 4-iodoaniline in a similar mannner to Example 4, obtained as an off-white powder (54%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 7.79 (s, 1H), 7.60 (d, 2H), 7.23 (d, 2H), 7.15 (s, 1H), 6.37 (s, 1H), 4.07 (t, 2H), 3.18 (t, 2H), 3.10 (br s, 4H), 2.61 (br s, 4H), 2.36 (s, 3H).

Description 44

N-[4-(Pyridin-4-yl)naphth-1-yl]acetamide

To a solution of 4-(pyridin-4-yl)naphth-1-ylamine (D2, 1.5g, 6.8mmole) in CH_2Cl_2 and triethylamine (1.0ml, 7.1mmole) at 0°C was added dropwise a solution of acetyl chloride (0.5ml, 7.0mmole) in CH_2Cl_2 (10ml) and the mixture stirred whilst allowing to warm to room temperature for 1h. The solution was washed with aqueous 10% Na_2CO_3, the organics dried (Na_2SO_4) and evaporated *in vacuo* to give the title compound as a yellow solid (1.9g, 100%).

^{1}H NMR (250 MHz,$CDCl_3$) δ(ppm): 8.73 (d, 2H), 7.99-7.40 (m, 8H), 2.37 (s, 3H). NH not observed.

Description 45

N-[4-(1-Methyl-1,2,5,6-tetrahydropyridin-4-yl)naphth-1-yl]acetamide

To a solution of N-[4-(pyridin-4-yl)naphth-1-yl]acetamide (D44, 1.8g, 6.8mmole) in acetone (50ml) was added iodomethane (1.92g, 13.6mmole) and the mixture left to stand overnight. Filtration gave a yellow solid (1.2g) which was dissolved in ethanol (25ml) and water (25ml), cooled to 0°C and treated portionwise with sodium borohydride (166mg, 4.4mmole) over 5min and then stirred for 1h. To the mixture was added aqueous 10% NaOH (16ml) and water (40ml), the product extracted with CH_2Cl_2, dried (Na_2SO_4) and evaporated *in vacuo* to give the title compound as a brown solid (880mg, 44%).

^{1}H NMR (250 MHz,$CDCl_3$) δ(ppm): 8.06 (dd, 1H), 7.86 (dd, 1H), 7.73 (d, 1H), 7.53 (m, 2H), 7.30 (s, 1H), 5.74 (m, 1H), 3.18 (br d, 2H), 2.75 (t, 2H), 2,56 (m, 2H), 2,47 (s, 3H), 2.32 (s, 3H). NH not observed.

Description 46

4-(1-Methylpiperidin-4-yl)naphth-1-ylamine

A solution of N-[4-(1-methyl-1,2,5,6-tetrahydropyridin-4-yl)naphth-1-yl]acetamide (D45, 800mg, 2.9mmole) in ethanol (50ml) was hydrogenated over 10% Pd-C at 50psi and 50°C for 192h. Filtration through celite and evaporation of the filtrate gave, on

evaporation, a white solid (683mg). The solid was dissolved in ethanol (10ml) and aqueous 2M NaOH (16ml) and heated at reflux under argon for 72h. The mixture was extracted with CH_2Cl_2, the organics dried (Na_2SO_4) and evaporated *in vacuo* to give the title compound as an orange oil (520mg, 76%).

^{1}H NMR (250 MHz,$CDCl_3$) δ(ppm): 8.06 (dd, 1H), 7.87 (dd, 1H), 7.53-7.40 (m, 2H), 7.22 (d, 1H), 6.78 (d, 1H), 4.06 (br s, 2H), 3.19 (m, 1H), 3.04 (br d, 2H), 2.36 (s, 3H), 2.20 (m, 2H), 1.92 (m, 4H).

Description 47

4-(4-Aminophenyl)-2-methyloxazole

A mixture of 2-methyl-4-(4-nitrophenyl)oxazole (1.70g, 8.2 mmole, J. Het. Chem. 1981, 18, 885) and 10% palladium on carbon (0.20g) in THF (70ml) was stirred under hydrogen at atmospheric pressure for 42h. The mixture was filtered and concentrated to dryness *in vacuo*. The residue was purified by chromatography on silica gel eluting with 2% MeOH in CH_2Cl_2. The title compound was obtained as a yellow powder (0.92g).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 7.66 (s, 1H), 7.52 (d, 2H), 6.70 (d, 2H), 3.73 (s, 2H), 2.49 (s, 3H).

Description 48

4-(2-Methyl-pyridin-4-yl)benzoic acid

The title compound was prepared from 4-bromo-2-methylpyridine (J. Org. Chem. 1985, 50, 4410) and 4-carboxyphenylboronic acid using a similar procedure to Description 2 as a white solid (84%).

^{1}H NMR (250 MHz, d^{6}DMSO) δ (ppm): 8.52 (d, 1H), 8.03 (d, 2H), 7.80 (d, 2H), 7.61 (s, 1H), 7.52 (dd, 1H), 2.55 (s, 3H). COOH not observed.

Description 49

4-(2-Methyl-pyridin-4-yl)aniline

The title compound was prepared from 4-(2-methyl-pyridin-4-yl)benzoic acid (D48) using a similar procedure to Description 1 to form the isocyanate, then by base hydrolysis using NaOH, to afford the amine as a beige solid (31%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.46 (d, 1H), 7.52 - 7.45 (m, 2H), 7.31 (s, 1H), 7.29 - 7.24 (m, 1H), 6.80 - 6.73 (m, 2H), 3.87 (s, 2H), 2.59 (s, 3H).

Description 50

N-(*tert*-Butyloxycarbonyl)-4-iodoaniline

To a solution of 4-iodoaniline (3g, 0.014 mole) in dry dichloromethane (20ml) was added di-*tert*-butyl dicarbonate (2.99g, 0.014 mole) followed by a catalytic amount of 4-dimethylaminopyridine. The reaction was stirred overnight at ambient temperature then washed with water (2x20ml) and dried ($MgSO_4$). Filtration and evaporation gave an off-white solid (1.90g, 43%).

^1H NMR (250MHz, $CDCl_3$) δ (ppm): 7.57 (d, 2H), 7.14 (d, 2H), 6.43 (br, 1H), 1.51(s, 9H).

Description 51

N-(*tert*-Butyloxycarbonyl)-4-(thiazol-2-yl)aniline

A mixture of N-(*tert*-butyloxycarbonyl)-4-iodoaniline (D50, 319mg, 1 mmole), bis (pinacolato)diboron (279mg, 1.1 mmole), 1,1'-bis(diphenylphosphino)ferrocene dichloropalladium (II) complex with DCM (1:1) (24mg, 0.029 mmole) and potassium acetate (294mg, 3 mmole) in dry DMF (6ml) was heated at 80°C for 2h. After cooling 2-bromothiazole (328mg, 2 mmole), 2M sodium carbonate (2.5ml) and 1,1'-bis (diphenylphosphino)ferrocene dichloropalladium (II) complex with DCM (1:1) (24mg, 0.029 mmole) was added and the reaction heated at 80°C for 18h. After cooling the solution was diluted with water (20ml). Extraction using ethyl acetate (2x20ml) followed by drying ($MgSO_4$), filtration and evaporation under reduced pressure gave an oil. This was chromatographed on silica gel eluting with 10% ethyl acetate in hexane to afford the title compound as an oil (137mg, 50%).

^1H NMR (250MHz, $CDCl_3$) δ (ppm): 7.91 (d, 2H), 7.82 (d, 1H), 7.48 (d, 2H), 7.27 (d, 1H), 6.62 (br, 1H), 1.54 (s, 9H).

Description 52

4-(Thiazol-2-yl)aniline

A solution of N-(*tert*-butyloxycarbonyl)-4-(thiazol-2-yl)aniline (D51, 122mg, 0.44 mmole) in dichloromethane (2ml) and trifluoroacetic acid (0.1ml) was stirred at ambient temperature for 18h and then water (20ml) was added. The aqueous phase was extracted with dichloromethane (2x10ml) and the extract washed with 10% aqueous sodium

hydrogen carbonate (2x20ml), then dried ($MgSO_4$) and evaporated under reduced pressure to give a light yellow oil, which solidified on standing (70mg, 90%).
^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 7.76 (m, 3H), 7.20 (d, 1H), 6.72 (d, 2H), 3.90 (br s, 2H).

Description 53

4-(Isoquinolin-2-yl)benzoic acid

The title compound was prepared from 4-carboxyphenylboronic acid and 4-bromoisoquinoline using a similar procedure to Description 2, obtained as an off-white solid (58%).
^{1}H NMR (250MHz, d^{6}DMSO) δ (ppm): 13.15 (br s, 1H), 9.39 (s, 1H), 8.49 (s, 1H), 8.25 (d, 1H), 8.13 (d, 2H), 7.90 - 7.67 (m, 5H).

Description 54

4-(Isoquinolin-4-yl)phenyl isocyanate

The title compound was prepared from 4-(isoquinolin-4-yl)benzoic acid (D53) using a similar procedure to Description 1. The isocyanate was used as its toluene solution without concentration to the neat compound.

Description 55

4-(Quinolin-3-yl)benzoic acid

The title compound was prepared from 4-carboxyphenylboronic acid and 3-bromoquinoline using a similar procedure to Description 2, obtained as a white solid (72%).
^{1}H NMR (250MHz, d^{6}DMSO) δ (ppm): 13.09 (br s, 1H), 9.32 (d, 1H), 8.76 (d, 1H), 8.07 (m, 5H), 7,83 (m, 2H), 7.67 (m, 1H).

Description 56

4-(Quinolin-3-yl)phenyl isocyanate

The title compound was prepared from 4-(quinolin-3-yl)benzoic acid (D55) using a similar procedure to Description 51. The isocyanate was used as its toluene solution without concentration to the neat compound.

Description 57

4-(Quinolin-8-yl)benzoic acid

The title compound was prepared from 4-carboxyphenylboronic acid and 8-bromoquinoline using a similar procedure to Description 2, obtained as a white solid (65%).

^{1}H NMR (250MHz, d^{6}DMSO) δ (ppm): 12.98 (br s, 1H), 8.92 (m, 1H), 8.46 (d, 1H), 8.06 (m, 3H), 7.80 (m, 4H), 7.60 (m, 1H).

Description 58

4-(Quinolin-8-yl)phenyl isocyanate

The title compound was prepared from 4-(quinolin-8-yl)benzoic acid (D57) using a similar procedure to Description 51. The isocyanate was used as its toluene solution without concentration to the neat compound.

Description 59

3-Bromo-2,6-dimethylpyridine (D59a) and 4-Bromo-2,6-dimethylpyridine (D59b)

A stirred solution of phosphorus oxybromide (25g, 0.085 mole) in 1,2-dichloroethane (250ml) at room temperature under argon was treated with 2,6-lutidine-N-oxide (10g, 0.081mole), then heated at reflux for 6h. The mixture was allowed to cool, then poured slowly into well stirred ice/water (400ml) and basified by addition of solid K_2CO_3. The aqueous mixture was extracted with dichloromethane and the extract dried (Na_2SO_4) and concentrated under vacuum. The residue was chromatographed on silica gel eluting with 1:1 ether /60-80 petrol to separate four components. The second component was 3-bromo-2,6-dimethylpyridine (2.5g, 21%) as a yellow oil;

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 7.66 (d, 1H), 6.86 (d, 1H), 2.63 (s, 3H), 2.48 (s, 3H)

and the third component was 4-bromo-2,6-dimethylpyridine (1.5g, 12%) as a pale yellow oil

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 7.16 (s, 2H), 2.50 (s, 6H).

Description 60

4-(2,6-Dimethyl-pyridin-4-yl)benzoic acid

The title compound was prepared from 4-bromo-2,6-dimethylpyridine (D59b) and 4-carboxyphenylboronic acid using a similar procedure to Description 2 as a white solid (76%).

^{1}H NMR (250MHz, d^{6}DMSO) δ (ppm): 8.05 (d, 2H), 7.86 (d, 2H), 7.42 (s, 2H), 2.50 (s, 6H). Acid proton not observed.

Description 61

4-(2,6-Dimethyl-pyridin-3-yl)benzoic acid

The title compound was prepared from 3-bromo-2,6-dimethylpyridine (D59a) and 4-carboxyphenylboronic acid using a similar procedure to Description 2 as a beige solid (76%).

^{1}H NMR (250MHz, d^6 DMSO) δ (ppm): 8.00 (d, 2H), 7.52 (d, 1H), 7.42 (d, 2H), 7.18 (d, 1H), 2.47 (s, 3H), 2.40 (s, 3H). Acid proton not observed.

Description 62

4-(2,6-Dimethyl-pyridin-4-yl)phenyl isocyanate

The title compound was prepared from 4-(2,6-dimethyl-pyridin-4-yl)benzoic acid (D60) using a similar procedure to Description 1. The isocyanate was used as its toluene solution without concentration to the neat compound.

Description 63

4-(2,6-Dimethyl-pyridin-3-yl)phenyl isocyanate

The title compound was prepared from 4-(2,6-dimethyl-pyridin-3-yl)benzoic acid (D61) using a similar procedure to Description 1. The isocyanate was used as its toluene solution without concentration to the neat compound.

Description 64

8-Bromo-5-nitroquinoline

8-Bromoquinoline (1.5g, 7.2 mmole) was added dropwise to a well stirred solution of conc. H_2SO_4 (5ml), conc. HNO_3 (10ml) and fuming HNO_3 (2ml), cooled in ice. The mixture was heated at 65°C for 30h, then cooled and poured into H_2O (350ml) with stirring. The precipitate that formed was filtered, washed

with H_2O and dried under vacuum to give the title compound as a pale cream solid (1.10g, 60%).

^1H NMR (250MHz, $CDCl_3$) δ (ppm): 9.17 (dd, 1H), 9.07 (dd, 1H), 8.26 (d, 1H), 8.20 (d, 1H), 7.74 (dd, 1H).

Description 65

5-Nitro-8-phenylquinoline

The title compound was prepared from 8-bromo-5-nitroquinoline (D64) and phenylboronic acid using a similar procedure to Description 2, as an orange/brown solid (99%).

^1H NMR (250MHz, $CDCl_3$) δ (ppm): 9.11 - 9.05 (m, 2H), 8.44 (d, 1H), 7.82 (d, 1H), 7.70 - 7.63 (m, 3H), 7.59 - 7.46 (m, 3H).

Description 66

5-Amino-8-phenylquinoline

The title compound was prepared from 5-nitro-8-phenylquinoline (D65) using a similar procedure to Description 20, as an orange/brown solid (97%).

^1H NMR (250MHz, $CDCl_3$) δ (ppm): 8.93 (dd, 1H), 8.21 (dd, 1H), 7.76 (dd, 1H), 7.66 (d, 1H), 7.59 - 7.32 (m, 5H), 6.89 (d, 1H), 4.23 (s, 2H).

Description 67

6-Acetamido-2-methylquinoline

The title compound was prepared from 6-amino-2-methylquinoline and acetic anhydride using a similar procedure to Description 8, as a green solid (95%).

^1H NMR (250MHz, $CDCl_3$) δ (ppm): 8.30 (d, 1H), 8.01 (d, 1H), 7.95 (d, 1H), 7.49 (m, 2H), 7.27 (d, 1H), 2.72 (s, 3H), 2.25 (s, 3H).

Description 68

6-Amino-2-(2-phenylethenyl)quinoline

A suspension of 6-acetamido-2-methylquinoline (D67, 600mg, 3.0 mmole) in acetic anhydride (6ml) was treated with benzaldehyde (954mg, 9.0 mmole) and the mixture heated at 120°C for 40h, then cooled and the acetic anhydride removed *in vacuo*. The residue was dissolved in 2M NaOH (30ml) and EtOH

(10ml) and heated under reflux with stirring. After 18h the EtOH was removed *in vacuo* and the residue extracted with EtOAc (3x100ml). The organics were combined, dried (Na_2SO_4) and concentrated *in vacuo* giving a crude brown oil, which was purified by chromatography on basic alumina eluting with EtOAc. The title compound was obtained as a brown solid (210mg, 28%), partially contaminated with benzyl alcohol.

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 7.91 - 7.87 (m, 2H), 7.60 - 7.56 (m, 2H), 7.54 (d, 1H), 7.42 - 7.28 (m, 5H), 7.15 (dd, 1H), 6.89 (d, 1H), 3.96 (s, 2H).

Description 69

6-Amino-2-(2-phenylethyl)quinoline

The title compound was prepared from 6-amino-2-(2-phenylethenyl)quinoline (D68) using a similar procedure to Description 20, as a yellow oil (41%), partially contaminated with benzyl alcohol.

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 7.87 (d, 1H), 7.80 (d, 1H), 7.38 - 7.08 (m, 7H), 6.89 (d, 1H), 3.90 (s, 2H), 3.25 - 3.07 (m, 4H).

Description 70

2-(3-Nitrophenoxy)pyrimidine

A stirred mixture of 3-nitrophenol (2.08g, 15 mmole), 2-bomopyrimidine (2.38g, 15 mmole) and anhydrous potassium carbonate (2.76g, 20 mmole) in dry DMF (20ml) was heated at 80°C for 4h. The cooled mixture was concentrated to dryness *in vacuo* and the residue partitioned between CH_2Cl_2 (75ml) and water (50ml). The organic phase was separated, washed with water, dried (Na_2SO_4) and concentrated to dryness *in vacuo*. The residue was purified by chromatography on silica gel eluting with CH_2Cl_2. The title compound was isolated as a pale yellow powder (1.94g, 60%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 8.60 (d, 2H), 8.14 (m, 2H), 7.58 (m, 2H), 7.12 (t, 1H).

Description 71

3-(Pyrimidin-2-yloxy)aniline

To a stirred mixture of 2-(3-nitrophenoxy)pyrimidine (D70, 0.65g, 3 mmole) and tin (II) chloride (2.28g, 12 mmole) in methanol (30ml) was added conc. HCl (0.7ml). The mixture was heated at reflux for 2h, cooled and concentrated *in vacuo* to near dryness. The residue was treated with CH_2Cl_2 (50ml) and water (25ml) and 2N NaOH solution was added to adjust the pH to 12. The mixture was filtered and the organic phase separated, washed with water, dried (Na_2SO_4) and concentrated to dryness *in vacuo* to afford the title compound as a yellow powder (0.50g, 89%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 8.55 (d, 2H), 7.19 (t, 1H), 7.02 (t, 1H), 6.59 - 6.51 (m, 3H), 3.76 (s, 2H).

Description 72

N-Methyl-4-nitro-N-(pyrimidin-2-yl)aniline

To a stirred solution of N-methyl-4-nitroaniline (2.20g, 14.5 mmole) in dry DMF (25ml) was added potassium *tert*-butoxide (1.79g, 16 mmole). After stirring for 1h at room temperature 2-bromopyrimidine (2.30g, 14.5 mmole) was added and the mixture warmed to 80°C for 6h and then stood overnight at room temperature. After concentrating to dryness *in vacuo*, the residue was partitioned between CH_2Cl_2 (100ml) and water (30ml). The organic phase was washed with water, dried (Na_2SO_4) and concentrated to dryness. Trituration of the residue in diethyl ether afforded the title compound as a pale yellow-orange powder (1.24g, 37%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 8.43 (d, 2H), 8.25 (d, 2H), 7.56 (d, 2H), 6.77 (t, 1H), 3.67 (s, 3H).

Description 73

4-[N-Methyl-N-(pyrimidin-2-yl)amino]aniline

A solution of N-methyl-4-nitro-N-(pyrimidin-2-yl)aniline (D72, 1.30g, 5.6 mmole) in methanol (70ml) and ethyl acetate (70ml) was treated with 10% palladium on carbon (0.25g), and shaken under hydrogen at 1 atmosphere for 48h. The filtered mixture was concentrated to dryness and the residue triturated in diethyl ether to afford the title compound as a pale orange-brown powder (0.78g, 68%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 8.30 (d, 2H), 7.07 (d, 2H), 6.68 (d, 2H), 6.48 (t, 1H), 3.66 (br s, 2H), 3.45 (s, 3H).

Description 74

5-(Pyridin-4-yl)naphth-1-ylamine

The title compound was prepared from 5-bromo-1-naphthylamine (JP 08151353A2) and 4-pyridylboronic acid using a similar procedure to Description 2.

^{1}H NMR (250MHz,$CDCl_3$) δ(ppm): 8.75-8.67 (m, 2H), 7.93 (d, 1H), 7.70-7.35 (m, 4H), 7.28-7.20 (m, 2H), 6.85-6.80 (m, 1H), 4.25 (s, 2H).

Description 75

N-[5-(Pyridin-4-yl)naphth-1-yl]acetamide

The title compound was prepared from 5-(pyridin-4-yl)naphth-1-ylamine (D74) in a similar manner to Description 44. MH^+ 263.

Description 76

N-[5-(1-Methyl-1,2,5,6-tetrahydropyridin-4-yl)naphth-1-yl]acetamide

The title compound was prepared from N-[5-(pyridin-4-yl)naphth-1-yl]acetamide (D75) in a similar manner to Description 45. MH^+ 281.

Description 77

5-(1-Methylpiperidin-4-yl)naphth-1-ylamine

The title compound was prepared from N-[5-(1-methyl-1,2,5,6-tetrahydropyridin-4-yl)-naphth-1-yl]acetamide (D76) in a similar manner to Description 46.

^{1}H NMR (250MHz,$CDCl_3$) δ(ppm):7.72 (m, 1H), 7.57 (d, 1H), 7.42 (m, 2H), 7.32 (t, 1H), 6.78 (d, 1H), 4.16 (br s, 2H), 3.28 (m, 1H), 3.05 (br d, 2H), 2.37 (s, 3H), 2.20 (m, 2H), 1.93 (m, 4H).

Description 78

N-2-(4-Nitrophenyl)ethyl-trifluoroacetamide

A solution of trifluoroacetic anhydride (10.6ml) in dichloromethane (100ml) was added dropwise to a stirred solution of 2,6-lutidine (17.4ml) and 4-nitrophenethylamine hydrochloride (15.2g, 75 mmole) at 0°C. The mixture was

stirred at 25°C overnight under argon and then washed with dilute citric acid (x2), brine and dried (Na_2SO_4). The material in the organic phase gave the title compound as a pale yellow solid (19.04g).

Description 79

7-Nitro-1,2,3,4-tetrahydro-2-trifluoroacetylisoquinoline

N-2-(4-Nitrophenyl)ethyl-trifluoroacetamide (D78, 2.26g, 9.15 mmole) and paraformaldehyde (0.45g, 14.4 mmole) in acetic acid (10ml) and conc. H_2SO_4 (15ml) were stirred at 25°C for 20h according to the procedure of G.E. Stokker, Tet. Lett., 1996, **37**, 5453. Work-up afforded the title compound as a white solid (2.17g).

^1H NMR (250MHz, $CDCl_3$) δ (ppm): 8.10 (m, 2H,), 7.38 (t, 1H), 4.92-4.85 (2 x s, 2H), 3.92 (m, 2H), 3.10 (m, 2H). MH^+ 274.

Description 80

7-Nitro-1,2,3,4-tetrahydroisoquinoline

7-Nitro-1,2,3,4-tetrahydro-2-trifluoroacetylisoquinoline (D79, 17.2g; 63 mmole) was hydrolysed at room temperature using a solution of potassium carbonate (46.6g) in 10% aqueous methanol (660ml). Work-up with dichloromethane gave the title compound (11g).

Description 81

2-Methyl-7-nitro-1,2,3,4-tetrahydroisoquinoline

7-Nitro-1,2,3,4-tetrahydroisoquinoline (D80, 2.08g; 11.7 mmole) was treated with 88% formic acid (3.45ml) and 37% aqueous formaldehyde (5.88ml) at 80°C for 2h according to the procedure of G.M. Carrera and D.S. Garvey, J. Het. Chem., 1992, **29**, 847. Basification with 10% sodium hydroxide followed by extraction with ethyl acetate afforded an orange gum (2.3g). Chromatography on silica gel in 0-3% methanol/ethyl acetate gave the title compound as an orange solid (1.7g). MH^+ 193.

Description 82

7-Amino-2-methyl-1,2,3,4-tetrahydroisoquinoline

2-Methyl-7-nitro-1,2,3,4-tetrahydroisoquinoline (D81, 0.25g; 1.3 mmole) in methanol (40ml) was hydrogenated over 10% palladium on carbon (100mg) at atmospheric pressure overnight. The catalyst was removed by filtration through a pad of kieselguhr and evaporation *in vacuo* gave the title compound as a white solid (213mg). MH^+ 163.

Description 83

8-Bromoquinoline-2,4-dicarboxylic acid

To a stirred solution of KOH (21.3g, 0.38 mole) in H_2O (64ml) was added 7-bromoisatin (10g, 0.044 mole, Proc. Royal Soc., 1958, 148, 481) over 1 min, followed by pyruvic acid (5.35ml, 0.077 mole) over 1 min. The resultant solution was stirred at room temperature for 1h, then heated under reflux for 1.5h, then cooled to room temperature, diluted with H_2O (100ml) and filtered. The filtrate was acidified to pH1 with conc. HCl acid, filtered, and the solid washed with H_2O and dried under vacuum. The title compound was a brown solid (10.1g, 77%).

^1H NMR (250 MHz, d^6 DMSO) δ(ppm) : 8.92 (dd, 1H), 8.64 (s, 1H), 8.44 (dd, 1H), 7.86 (t, 1H). Acid protons not observed.

Description 84

8-Bromoquinoline-4-carboxylic acid

A solution of 8-bromoquinoline-2,4-dicarboxylic acid (D83, 10g, 34 mmole) in nitrobenzene (40ml) was heated under reflux for 2h, then allowed to cool to room temperature, diluted with hexane (60ml) and the title compound filtered off as a brown solid (8.5g, 100%).

^1H NMR (250 MHz, d^6 DMSO) δ(ppm) : 8.95 (d, 1H), 8.50 (dd, 1H), 8.04 (dd, 1H), 7.82 (d, 1H), 7.44 (t, 1H). Acid proton not observed.

Description 85

8-Phenylquinoline-4-carboxylic acid

The title compound was prepared from 8-bromoquinoline-4-carboxylic acid (D 84) and phenylboronic acid using a similar procedure to Description 2, as a brown solid (63%).

^1H NMR (250 MHz, $CDCl_3$) δ (ppm) : 9.12 (d, 1H), 8.89 (dd, 1H), 8.05 (d, 1H), 7.84-7.73 (m,2H), 7.68-7.64 (m, 2H), 7.54-7.40 (m, 3H). Acid proton not discernible.

Description 86

8-Phenylquinolin-4-yl isocyanate

The title compound was prepared from 8-phenylquinoline-4-carboxylic acid (D 85) using a similar procedure to Description 1. The isocyanate was used as its toluene soloution without concentration to the neat compound.

Description 87

4-Amino-2-methylphenylboronic acid

A stirred solution of 4-bromo-3-methylaniline (20g, 0.107 mole) and triethylamine (33ml, 0.237 mole) in dichloromethane (250ml) at 0°C under argon was treated dropwise over 15 min with a solution of bis(chlorodimethylsilyl)ethane (25.3g, 0.12 mole) in dichloromethane (100ml). The mixture was warmed to room temperature and stirred for 20h, then filtered and concentrated *in vacuo*. The residue was extracted with 60-80 petrol (400ml) and the filtrate concentrated *in vacuo* to leave the stabase as an orange oil (35g, 100%). This was dissolved in dry THF (400ml), coled to -65°C under argon and treated dropwise over 15 min with 2.5M n-butyllithium in hexane (52ml, 0.13mole). The mixture was stirred at -65°C for 1h, then treated dropwise over 10 min with triisopropylborate (30ml, 0.13 mole), stirred at -65°C for a further 1.5h, then treated with saturated aqueous NH_4Cl solution (100ml) and allowed to warm to room temperature. The mixture was diluted with water (200ml), acidified with conc. HCl acid (50ml), stirred for 20 min, then concentrated under vacuum to approx. 400ml volume. The aqueous residue was washed with ethyl acetate and then basified by addition of solid K_2CO_3. The basic mixture was extracted with ethyl acetate and the extract dried (Na_2SO_4) and concentrated under vacuum to approx. 150ml volume, when a solid began to precipitate out. The mixture was cooled to 8°C and the solid filtered off and dried to afford the title compound as a white solid (9.2g, 51%).

^{1}H NMR (250MHz, d^{6}DMSO) δ (ppm): 7.69 (d, 1H), 6.40-6.32 (m, 2H), 5.34 (br s, 2H), 2.52 (s, 3H). Acid protons not observed.

Description 88

4-(2,6-Dimethyl-pyridin-4-yl)-3-methylaniline

The title compound was prepared from 4-chloro-2,6-dimethylpyridine (Chem. Abs. 1952, **46**, 4541) and 4-amino-2-methylphenylboronic acid (D87) using a similar procedure to Description 2 as beige solid (4%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 7.01 (d, 1H), 6.90 (s, 2H), 6.62-6.54 (m, 2H), 3.70 (br s, 2H), 2.55 (s, 6H), 2.22 (s, 3H).

Description 89

3-Methyl-4-(6-methyl-pyridin-2-yl)aniline

The title compound was prepared from 2-bromo-6-methylpyridine and 4-amino-2-methylphenylboronic acid (D87) using a similar procedure to Description 2 as beige solid (100%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 7.62-7.55 (m, 1H), 7.22 (d, 1H), 7.15 (d, 1H), 7.05 (d, 1H), 6.62-6.55 (m, 2H), 3.68 (br s, 2H), 2.59 (s, 3H), 2.31 (s, 3H).

Description 90

5-Carboxy-naphth-1-ylboronic acid

A stirred solution of 5-bromo-1-naphthoic acid (Bull. Soc. Chim. Fr., 1968, **7**, 2957, 22.3g, 0.089 mole) in dry THF (1000ml) at -60°C under argon was treated dropwise over 15 min with 1.6M n-butyllithium in hexane (125ml, 0.20 mole). The initial brown solution gave a beige precipitate as the first equivalent was added, which redissolved on addition of the second equivalent. The resulting solution was stirred at -60°C for 40 min, then triisopropylborate (51ml, 0.22 mole) was added, and the mixture stirred at -60°C for a further 1h, before warming gradually to -10°C. Saturated aqueous NH_4Cl solution was added (300ml), followed by water (400ml) and then 5M HCl acid (200ml). The resulting mixture was concentrated *in vacuo* to approx. 1000ml volume, then basified by addition of 40% NaOH solution and washed with ethyl acetate. The aqueous was added to excess 5M HCl acid and the solid which precipitated out was filtered off, washed with water and dried to afford a white solid (9.67g), which contained approx. 50% of the title compound together with 1-naphthoic acid.

Description 91

5-(6-Methyl-pyridin-2-yl)-1-naphthoic acid

The title compound was prepared from 2-bromo-6-methylpyridine and 5-carboxy-naphth-1-ylboronic acid (D90) using a similar procedure to Description 2 as beige solid (46%). ^{1}H NMR (250MHz, d^{6}DMSO) δ (ppm): 8.90 (d, 1H), 8.13 (d, 1H), 8.06 (dd, 1H), 7.84 (t, 1H), 7.67 (t, 1H), 7.62-7.46 (m, 2H), 7.41 (d, 1H), 7.32 (d, 1H), 2.55 (s, 3H). Acid proton not observed.

Description 92

5-(6-Methyl-pyridin-2-yl)naphth-1-yl isocyanate

The title compound was prepared from 5-(6-methyl-pyridin-2-yl)-1-naphthoic acid (D91) using a similar procedure to Description 1. The isocyanate was not isolated, but used in the next step as its toluene solution.

Description 93

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-trifluoroacetyl-1H-indole

The title compound was prepared from 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Description 31, as a beige solid (96%). ^{1}H NMR (250 MHz, CDCl3) δ (ppm) : 8.02 (s, 1H), 7.25 (s, 1 H), 4.29 (t, 2H), 3.19 (t, 2H), 3.10 (br s, 4H), 2.64 (br s, 4H), 2.39 (s, 3H).

Description 94

5-Chloro-2,3-dihydro-6-(piperazin-1-yl)-1-trifluoroacetyl-1H-indole

To a stirred soloution of 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)trifluoroacetyl-1H-indole (D93, 7.0g, 20 mmole) in 1,2-dichloroethane (200ml) under argon, was added diisopropylethylamine (3.50ml, 20 mmole) followed by 1-chloroethyl chloroformate (4.35ml, 40mmole). After 1h the mixture was washed with dilute $NaHCO_3$ (aq), then dried (Na_2SO_4) and concentrated *in vacuo* giving a brown solid (8.86g, 100%). A suspension in MeOH (200ml) was stirred under reflux for 3h, then allowed to cool and the MeOH removed *in vacuo*. The residue was partitioned between dilute $NaHCO_3$ (aq) and CH_2Cl_2. The CH_2Cl_2 was seperated and the aqueous reextracted with CH_2Cl_2 (2 x 50ml). The organics were combined, dried (Na_2SO_4) and concentrated *in vacuo* giving the title compound as a brown solid (4.79g, 72%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm) : 8.00 (s, 1H), 7.25 (s, 1H), 4.30 (t, 2H), 3.20 (t, 2H), 3.10-3.08 (br m, 8 H). NH not disernible.

Description 95

6-(4-Acetylpiperazin-1-yl)-5-chloro-2,3-dihydro-1-trifluoroacetyl-1H-indole

A stirred soloution of 5-chloro-2,3-dihydro-6-(piperazin-1-yl)-1-trifluoroacetyl-1H-indole (D 94, 1.0g, 3.0 mmole) in CH_2Cl_2 (50ml) cooled in ice, was treated with acetic anhydride (0.34g, 3.3 mmole) then allowed to warm to room temperature. After 6h the mixture was washed with dilute $NaHCO_3$ (aq), dried (Na_2SO_4) and concentrated *in vacuo* to afford the title compound as a brown solid (1.10g, 97%).

^1H NMR (250 MHz, $CDCl_3$) δ (ppm) : 7.98 (s, 1H), 7.26 (s, 1H), 4.31 (t, 2H), 3.79 (br s, 2H), 3.64 (br s, 2H), 3.21 (t, 2H), 3.05-3.00 (m, 4H), 2.15 (s, 3H).

Description 96

6-(4-Acetylpiperazin-1-yl)-5-chloro-2,3-dihydro-1H-indole

The title compound was prepared from 6-(4-acetylpiperazin-1-yl)-5-chloro-2,3-dihydro-1-trifluoroacetyl-1H-indole (D 95) using a similar procedure to Description 33, as a brown foam (81%).

^1H NMR (250 MHz, $CDCl_3$) δ (ppm) : 7.09 (s, 1H), 6.33 (s, 1H), 3.79-3.75 (m, 2H), 3.63-3.54 (m,4H), 3.01-2.91 (m, 6H), 2.13 (s, 3H). NH not discernible.

Description 97

5-Chloro-2,3-dihydro-6-(4-ethylpiperazin-1-yl)-1H-indole

A stirred solution of 6-(4-acetylpiperazin-1-yl)-5-chloro-2,3-dihydro-1H-indole (D96, 0.65g, 2.3 mmole) in THF (30ml) at room temperature under argon was treated with 1M borane-THF complex in THF (9.3ml, 9.3 mmole), then heated at reflux for 5h. The mixture was cooled to 0°C then treated dropwise with conc HCl acid (6ml) in methanol (25ml). After 30 min, the solution was heated to reflux for 2h, then concentrated *in vacuo*. The residue was treated with ethyl acetate (50ml) and 2M HCl acid (40ml), shaken well and the aqueous layer separated, basified with K_2CO_3 and extracted with dichloromethane. The extract was dried (Na_2SO_4), concentrated *in vacuo* and the residue purified by chromatography on silica gel eluting with 2-10% methanol/dichloroemethane to afford the title compound as a beige solid (0.31g, 50%).

^1H NMR (250MHz, $CDCl_3$) δ (ppm): 7.07 (s, 1H), 6.41 (s, 1H), 3.73 (br s, 1H), 3.56 (t, 2H), 3.03 (br s, 4H), 2.97 (t, 2H), 2.63 (br s, 4H), 2.49 (q, 2H), 1.13 (t, 3H).

Description 98

6-[4-(*tert*-Butyloxycarbonyl)piperazin-1-yl]-5-chloro-2,3-dihydro-1-trifluoroacetyl-1H-indole

The title compound was prepared from 5-chloro-2,3-dihydro-6-(piperazin-1-yl)-1-trifluoroacetyl-1H-indole (D94) and di-*tert*-butyl dicarbonate using a similar procedure to Description 95, as a brown foam (100%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 7.99 (s, 1H), 7.26 (s, 1H), 4.30 (t, 2H), 3.60 (t, 4H), 3.20 (t, 2H), 2.98 (t, 4H), 1.49 (s, 9H).

Description 99

6-[4-(*tert*-Butyloxycarbonyl)piperazin-1-yl]-5-chloro-2,3-dihydro-1H-indole

The title compound was prepared from 6-[4-(*tert*-butyloxycarbonyl)piperazin-1-yl]-5-chloro-2,3-dihydro-1-trifluoroacetyl-1H-indole (D98) using a similar procedure to Description 33, as a brown solid (84%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 7.08 (s, 1H), 6.35 (s, 1H), 3.60 - 3.53 (m, 6H), 3.01 - 2.89 (m, 6H), 1.48 (s, 9H), NH not discernible.

Description 100

6-[4-(*tert*-Butyloxycarbonyl)piperazin-1-yl]-5-chloro-2,3-dihydro-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole

The title compound was prepared from 4-(pyridin-4-yl)naphth-1-ylamine (D2) and 6-[4-(*tert*-butyloxycarbonyl)piperazin-1-yl]-5-chloro-2,3-dihydroindole (D99) using a similar procedure to Example 4, as a yellow/brown solid (67%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 8.74 (d, 2H), 7.99 (d, 1H), 7.91 - 7.86 (m, 3H), 7.67 - 7.41 (m, 5H), 7.21 (s, 1H), 6.81 (s, 1H), 4.31 (t, 2H), 3.56 (t, 4H), 3.30 (t, 2H), 2.96 (t, 4H), 1.46 (s, 9H).

Description 101

6-[4-(*tert*-Butyloxycarbonyl)piperazin-1-yl]-5-chloro-2,3-dihydro-1-[5-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole

The title compound was prepared from 5-(pyridin-4-yl)naphth-1-ylamine (D74) and 6-[4-(*tert*-butyloxycarbonyl)piperazin-1-yl]-5-chloro-2,3-dihydro-1H-indole (D99) using a similar procedure to Example 4, as a yellow/brown solid (74%).
^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 8.75 (d, 2H), 8.02 (d, 1H), 7.85 (s, 1H), 7.78 - 7.42 (m, 7H), 7.21 (s, 1H), 6.74 (s, 1H), 4.30 (t, 2H), 3.56 (t, 4H), 3.30 (t, 2H), 2.95 (t, 4H), 1.45 (s, 9H).

Description 102

4-(Pyridazin-3-yl)benzoic acid

The title compound was prepared from 3-chloropyridazine and 4-carboxyphenylboronic acid using a similar procedure to Description 24 as a brown solid (87%). MS: m/z = 199 (M-H).

Description 103

4-(Pyrazin-2-yl)benzoic acid

The title compound was prepared from 2-chloropyrazine and 4-carboxyphenylboronic acid using a similar procedure to Description 24 as a white solid (88%). MS: m/z = 156 ($M-CO_2$).

Description 104

6-Phenylnicotinic acid

The title compound was prepared from 6-chloronicotinic acid and phenylboronic acid using a similar procedure to Description 24 as an off white solid (54%). MS: m/z = 200 (MH^+).

Description 105

4-(6-Methyl-pyridazin-3-yl)benzoic acid

The title compound was prepared from 3-chloro-6-methylpyridazine and 4-carboxyphenylboronic acid using a similar procedure to Description 24 as a yellow solid (52%). MS: m/z = 213 (M-H).

Description 106

4-(4-Cyano-3-methylphenyl)benzoic acid

The title compound was prepared from 4-bromo-2-methylbenzonitrile and 4-carboxyphenylboronic acid using a similar procedure to Description 24 as a white solid (75%). MS: m/z = 236 (M-H).

Description 107

4-(5-Methyl-oxazol-2-yl)aniline

A mixture of 5-methyl-2-(4-nitrophenyl)oxazole (Chim. Ther. 1973, **8(4)**, 437) (3.0g, 15mmole) and 10% palladium on carbon (0.25g) in THF (75ml) was stirred under an atmosphere of hydrogen for 24h. The mixture was filtered and concentrated *in vacuo* to dryness to afford the title compound as a pale buff powder (2.29g, 89%).
^{1}H NMR (250 MHz, d^{6}DMSO) δ (ppm): 7.70 (d, 2H), 7.15 (s, 1H), 6.73 (d, 2H), 5.74 (s, 2H), 2.42 (s, 3H).

Description 108

5-Nitro-naphth-1-ylcarboxamide

A stirred suspension of 5-nitro-naphth-1-ylcarboxylic acid (Chem. Pharm. Bull 1984, **32(10)**, 3968) (3.50g, 16mmole) in CH_2Cl_2 (200ml) was treated with oxalyl chloride (2.1 ml, 24 mmole) and DMF (2 drops). The mixture was stirred at room temperature for 5h. The solution was concentrated to dryness *in vacuo*, and the residue dissolved in dry THF (200ml). Ammonia was slowly bubbled through the solution for 0.5h. The mixture was concentrated to dryness *in vacuo* and the residue triturated in water, and the solid filtered off and dried *in vacuo* to afford the title compound as a pale brown powder (3.34g, 95%).
^{1}H NMR (250 MHz, d^{6}DMSO) δ(ppm): 8.47 (d, 1H), 8.23-8.13 (m, 2H), 8.05 (s, 1H) 7.71-7.59 (m, 4H).

Description 109

N-[1-(Dimethylamino)ethylidene]-5-nitronaphth-1-ylcarboxamide

A stirred mixture of 5-nitro-naphth-1-ylcarboxamide (D108, 1.50g, 7 mmole) and N,N-dimethylacetamide dimethylacetal (3ml) was heated to 110°C for 2 h. The cooled mixture was diluted with water (20ml) and the precipitated solid filtered off, washed with water and dried *in vacuo* to afford the title compound as a pale brown powder (1.60g, 80%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 9.31 (d, 1H), 8.53 (d, 1H), 8.22 (dd, 1H) 8.15 (dd, 1H), 7.72-7.56 (m, 2H), 3.19 (d, 6H), 2.45 (s, 3H).

Description 110

3-Methyl-5-(5-nitro-naphth-1-yl)-1,2,4-oxadiazole

To a stirred solution of hydroxylamine hydrochloride (0.47g, 6.75 mmole) and 5M NaOH solution (1.35 ml, 6.75 mmole) in 70% aqueous acetic acid (10 ml) was added N-[1-(dimethylamino)ethylidene]-5-nitronaphth-1-ylcarboxamide (D109, 1.55g, 5.4 mmole). The mixture was warmed to 80°C for 4h, then cooled and diluted with water (50ml). The precipitated solid was filitered off, washed with water and dried *in vacuo* to leave the title compound as a pale buff powder (1.11g, 80%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 9.52 (d, 1H), 8.71 (d, 1H), 8.44 (dd, 1H) 8.25 (dd, 1H), 7.87-7.73 (m, 2H), 2.59 (s, 3H).

Description 111

5-(3-Methyl-1,2,4-oxadiazol-5-yl)naphth-1-ylamine

The title compound was prepared from 3-methyl-5-(5-nitronaphth-1-yl)-1,2,4-oxadiazole (D110) using a similar procedure to Description 71 as a pale yellow powder (54%).

^{1}H NMR (250 MHz $CDCl_3$) δ (ppm): 8.52 (d, 1H), 8.30 (dd, 1H), 8.09 (d, 1H), 7.58-7.44 (m, 2H), 6.88 (dd, 1H), 4.23 (s, 2H) 2.56 (s, 3H).

Description 112

5-Nitro-N-propargylnaphth-1-ylcarboxamide

A stirred suspension of 5-nitronaphth-1-ylcarboxylic acid (Chem. Pharm Bull. 1984, **32(10)**, 3986) (1.10g, 5 mmole) in CH_2Cl_2 (50ml) was treated with oxalyl chloride (0.5 ml, 6 mmole) and DMF (1 drop). After 3h at room temperature the mixture was concentrated to dryness *in vacuo*. The residue was dissolved in CH_2Cl_2 (30ml), treated with triethylamine (1.4nl, 10 mmole) followed with dropwise addition of a solution of propargylamine (0.28g, 5 mmole) in CH_2Cl_2 (10ml). After stirring at room temperature for 18h the mixture was washed with water, dried (Na_2SO_4) and concentrated to dryness *in vacuo*. The residue was triturated in diethyl ether to afford the title compound as a pale yellow powder (0.79g, 61%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.62 (t, 2H), 8.24 (d, 1H), 7.73-7.59 (m, 3H), 6.30 (s, 1H) 4.34 (dd, 2H), 2.33 (t, 1H).

Description 113

5-Methyl-2-(5-nitronaphth-1-yl)oxazole

A stirred mixture of 5-nitro-N-propargylnaphth-1-ylcarboxamide (D112, 0.75g, 3 mmole) and mercuric acetate (0.04g, 0.12 mmole) in glacial acetic acid (10 ml) was heated to reflux for 4h. The cooled mixture was concentrated to dryness *in vacuo*, and the residue dissolved in CH_2Cl_2, washed with aq. K_2CO_3 solution, dried (Na_2SO_4) and concentrated to dryness *in vacuo*. The residue was subjected to flash chromatography on silica gel eluting with CH_2Cl_2 to afford the title compound as a yellow powder (0.50g, 66%).
^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 9.75 (d, 1H), 8.54 (d, 1H), 8.26 (d, 1H), 8.19 (d, 1H), 7.79-7.64 (m, 2H), 7.01 (s, 1H), 2.47 (s, 3H).

Description 114

5-(5-Methyloxazol-2-yl)naphth-1-ylamine

The title compound was prepared from 5-methyl-2-(5-nitronaphth-1-yl)oxazole (D113) using a similar procedure to Description 28, obtained as a yellow/green gum (95%).
^{1}H NMR (250 MHz, d^6DMSO) δ (ppm): 8.64 (d, 1H), 8.11 (dd, 1H), 7.94 (d, 1H), 7.53-7.39 (m, 2H), 6.97 (d, 1H), 6.48 (d, 1H), 4.18 (s, 2H), 2.45 (s, 3H).

Description 115

3-Methyl-4-(pyrimidin-2-yl)aniline

The title compound was prepared from 2-bromopyrimidine and 4-amino-2-methylphenyl boronic acid (D87) using a similar procedure to Descripton 2 as yellow solid (46%).
^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.76 (d, 2H), 7.75 (d, 1H), 7.11 (t, 1H), 6.62 (d, 1H), 6.59 (s, 1H), 3.78 (br, 2H), 2.55 (s, 3H).

Description 116

3-Methyl-4-(pyrimidin-5-yl)aniline

The title compound was prepared from 5-bromopyrimidine and 4-amino-2-methylphenylboronic acid (D87) using a similar procedure to Description 2 as a straw coloured solid (91%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 9.14 (s, 1H), 8.70 (s, 2H), 7.67 (m, 1H), 7.01 (d, 1H), 6.65 (s, 1H), 6.62 (d, 1H), 3.60 (br, 2H), 2.23 (s, 3H).

Description 117

2,6-Dimethyl-4-iodopyridine

A sirred solution of 4-chloro-2,6-dimethylpyridine (Chem. Abs. 1952, **46**, 4541) (2.6g, 18 mmole) in 2-butanone (250ml) was treated with sodium iodide (17.6g, 120 mmole) and 4-toluenesulphonic acid (3.4g, 18 mmole) and the mixture heated at reflux under argon for 72h. The reaction mixture was cooled, then concentrated *in vacuo* and the residue was treated with water (200ml) and extracted with ethyl acetate. The extract was washed with aqueous sodium thiosulphate solution, then dried (Na_2SO_4) and concentrated *in vacuo* to afford the title compound as a white solid, which was converted to its hydrochloride salt as a white solid from acetone (3.44g, 69%).

^{1}H NMR (free base) (250 MHz, $CDCl_3$) δ (ppm): 7.37 (s, 2H), 2.46 (s, 6H). $MH^+ = 234$.

Description 118

5-(2,6-Dimethyl-pyridin-4-yl)-1-naphthoic acid

The title compound was prepared from 2,6-dimethyl-4-iodopyridine (D117) and 5-carboxynaphth-1-ylboronic acid (D90) using a similar procedure to Description 2 as a white solid (70%).

^{1}H NMR (250 MHz, d^{6}DMSO) δ (ppm): 8.75 (d, 1H), 7.99 (dd, 1H), 7.80 (d, 1H), 7.60-7.52 (m, 1H), 7.50-7.32 (m, 2H), 7.00 (s, 2H), 2.36 (s, 6H). Acid proton not observed.

Description 119

5-(2,6-Dimethyl-pyridin-4-yl)naphth-1-yl isocyanate

The title compound was prepared from 5-(2,6-dimethyl-pyridin-4-yl)-1-naphthoic acid (D118) using a similar procedure to Description 1. The isocyanate was not isolated, but used as its toluene solution in the next step.

Description 120

4-(2,6-Dimethylpyridin-3yl)-3-methylaniline

The title compound was prepared from 3-bromo-2,6-dimethylpyridine (D59a) and 4-amino-2-methylphenylboronic acid (D87) using a similar procedure to Description 2 as a pale yellow oil (6.5%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 7.32-7.25 (m, 1H), 7.00 (d, 1H), 6.87 (d, 1H), 6.65-6.52 (m, 2H), 3.67 (br s, 2H), 2.56 (s, 3H), 2.28 (s, 3H), 1.98 (s, 3H).

Description 121

3-Methyl-4-(thiazol-2-yl)aniline

The title compound was prepared from 2-bromothiazole and 4-amino-2-methylphenylboronic acid (D87) using a similar procedure to Description 2 as a yellow/brown oil (65%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.83 (d, 1H), 7.57 (d, 1H), 7.28 (m, 1H), 6.57 (m, 2H), 3.80 (br, 2H), 2.53 (s, 3H).

Description 122

5-(Pyrimidin-5-yl)-1-naphthoic acid

The title compound was prepared from 5-bromopyrimidine and 5-carboxynaphth-1-ylboronic acid (D90) using a similar procedure to Description 2 as a beige solid (78%).

^{1}H NMR (250 MHz, d^6DMSO) δ (ppm): 13.30 (br, 1H), 9.35 (s, 1H), 9.00 (s, 2H), 8.96 (d, 1H), 8.19 (d, 1H), 7.93 (d, 1H), 7.78 (m, 1H),7.65 (m, 2H).

Description 123

5-(Pyrimidin-5-yl)naphth-1-yl isocyanate

The title compound was prepared from 5-(pyrimidin-5-yl)-1-naphthoic acid (D122) using a similar procedure to Decsription 1. The isocyanate was not isolated, but used as its toluene solution in the next step.

Description 124

5-Acetylnaphth-1-ylamine

A stirred solution of 1-acetyl-5-nitronaphthalene (Aust. J. Chem. 1995, **48(12)**, 1969) (0.75g, 3.5 mmole), 10% Pd-C (0.20g) and cyclohexene (10 ml) in methanol (75 ml) was heated under reflux for 6h. The cooled mixture was filtered and concentrated *in vacuo*. The residue was dissolved in CH_2Cl_2 (50 ml), washed with water, dried (Na_2SO_4) and

concentrated to dryness. Trituration of the residue with ether/hexane afforded the title compound as a yellow/brown powder (0,52g, 80%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.03 (t, 2H), 7.83 (dd, 1H), 7.49-7.36 (m, 2H), 6.83 (d, 1H), 4.17 (s, 2H), 2.73 (s, 3H).

Description 125

5-(Pyrimidin-2-yloxy)naphth-1-ylamine

The title compound was prepared from 5-hydroxynaphth-1-ylamine and 2-bromopyrimidine using a similar procedure to Description 70, as a pale buff coloured powder (58%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.52 (d, 2H), 7.73 (d, 1H), 7.48 (t, 1H), 7.40-7.21 (m, 3H), 7.01 (t, 1H), 6.78 (d, 1H), 4.13 (s, 2H).

Description 126

5-Cyanonaphth-1-ylamine

To a stirred suspension of 5-nitronaphth-1-ylcarbonitrile (D128, 0.15g, 0.76 mmole) in ethanol (10ml) and water (5ml) was added iron powder (0.21g, 3.7 mmole) and ammonium chloride (0.02g, 0.4 mmole), then the mixture was heated under reflux for 0.5h. The mixture was cooled slightly, filtered and concentrated *in vacuo*. The residue was partitioned between ethyl acetate (25ml) and water (15ml). The organic layer was separated, dried (Na_2SO_4) and concentrated to dryness to afford the title compound as a yellow/green powder (0.11g, 85%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.06 (d, 1H), 7.88 (d, 1H), 7.68 (d, 1H), 7.49 (m, 2H), 6.88 (d, 1H), 4.27 (s, 2H).

Description 127

5-Nitronaphth-1-ylcarbonitrile

To stirred solution of 5-nitronaphth-1-ylcarboxamide (D108, 0.20g, 0.93mmole) in CH_2Cl_2 (10ml) was added 2.5M solution of trimethylsilylphosphate in CH_2Cl_2 (5ml) (Synthesis, 1982, 591) and the mixture heated to reflux for 2h. The cooled mixture was treated with water (10ml) and after stirring for 10 min the organic phase was separated, washed with brine, dried (Na_2SO_4) and concentrated to dryness *in vacuo*. The residue

was subjected to flash chromatography on silica gel eluting with CH_2Cl_2 to afford the title compound as a colourless powder (0.12g, 66%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.82 (d, 1H), 8.57 (d, 1H), 8.35 (d, 1H), 8.06 (d, 1H), 7.83 (m, 2H)

Description 128

5-Nitronaphth-1-ylamidoxime

To a solution of sodium hydroxide (0.71g, 17.8mmole) in methanol (100ml) was added hydroxylamine hydrochloride (1.23g, 1.78mmole). The mixture was treated with 5-nitronaphth-1-ylcarbonitrile (D127, 1.60g, 8.1mmole) and heated to reflux for 48h. The cooled mixture was concentrated by evaporation to 10ml and then treated with water (50ml). The precipitate was collected, washed with water and dried *in vacuo* to afford the title compound as a pale yellow powder (1.65g, 88%).

^{1}H NMR (250 MHz, d^{6}DMSO) δ (ppm): 9.74 (s, 1H), 8.66 (d, 1H), 8.30 (m, 2H), 7.86-7.72 (m, 3H), 6.14 (s, 2H).

Description 129

5-Methyl-3-(5-nitronaphth-1-yl)-1,2,4-oxadiazole

To a stirred solution of 5-nitronaphth-1-ylamidoxime (D128, 1.28g, 5.5mmole) in pyridine (10ml) was added dropwise acetyl chloride (0.78ml, 11mmole). The mixture was stirred at room temperature for 0.5h, then heated to reflux for 24h. The cooled mixture was treated with water (100ml) and extracted with ethyl acetate (3x25ml). The combined organic extracts were washed with dilute HCl, water, dried (Na_2SO_4) and concentrated to dryness. The residue was subjected to flash chromatography on silica gel eluting with CH_2Cl_2 to afford the title compound as a pale yellow powder (0.86g, 61%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 9.27 (d, 1H), 8.63 (d, 1H), 8.36, (dd, 1H), 8.24 (dd, 1H), 7.81 (q, 1H), 7.69 (q, 1H), 2.75 (s, 3H).

Description 130

5-(5-Methyl-1,2,4-oxadiazol-3-yl)naphth-1-ylamine

The title compound was prepared according to the procedure outlined in Description 126, as brown gum. This was converted to its hydrochloride salt to afford a grey powder.

^{1}H NMR (HCl salt) (250 MHz, CD_3OD) δ (ppm): 8.72 (t, 1H), 8.08 (dd, 1H), 7.91 (d, 1H), 7.60 (dd, 1H), 7.44 (d, 2H), 4.63 (s, 2H), 2.46, (s, 3H).

Example 1

1-[(4-Bromo-3-methylphenyl)aminocarbonyl]-5-methoxy-6-(4-methylpiperazin-1-yl)indole

To a solution of 5-methoxy-6-(4-methylpiperazin-1-yl)indole (130mg, 0.50 mmole, intemediate 2 in WO95/06637) in anhydrous THF (10ml) under argon, was added potassium t-butoxide (59mg, 0.50 mmole) and the mixture stirred for 15 min. To this was added a solution of 4-bromo-3-methylphenyl isocyanate (D1, 127mg, 0.60 mmole) in anhydrous THF (10ml). The resulting mixture was stirred under argon at room temperature for 16h, then concentrated *in vacuo*. The residue was purified by column chromatography on silica gel eluting with 0-6% MeOH/CH_2Cl_2 to afford the title compound as a pale yellow solid (108mg, 45%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm):7.67 (s, 1H), 7.34 (d, 1H), 7.30 (d, 1H), 7.21 (d, 1H), 7.15 (s, 1H), 7.05 (dd, 1H), 6.86 (s, 1H), 6.42 (d, 1H), 3.76 (s, 3H), 3.03 (br s, 4H), 2.59 (br s, 4H), 2.25 (s, 6H).

Example 2

1-[(4-Bromo-3-methylphenyl)aminocarbonyl]-2,3-dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole

2,3-Dihydro-5-methoxy-6-(4-methylpiperzin-1-yl)-1H-indole (0.10g, 0.40 mmole, intermediate 3 in WO 95/06627) in dichloromethane (10ml) was added to a solution of 4-bromo-3-methylphenyl isocyanate (D1, 0.11g, 0.50 mmole) in dichloromethane (10ml). The mixture was stirred at room temperature for 17h, then concentrated *in vacuo* to afford a dark yellow oil. This oil was stirred with diethyl ether producing the title compound as a yellow solid, which was filtered off and dried (0.17g, 92%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm):7.59 (s, 1H), 7.36 (d, 1H), 7.29 (d, 1H), 7.03 (dd, 1H), 6.65 (s, 1H), 6.25 (s, 1H), 3.98 (t, 2H), 3.76 (s, 3H), 3.13 (t, 2H), 3.05 (br s, 4H), 2.54 (br s, 4H), 2.30 (s, 3H), 2.28 (s, 3H).

Example 3

1-[(2,3-Dichlorophenyl)aminocarbonyl]-2,3-dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 2,3-dichlorophenyl isocyanate and 2,3-dihydro-5-methoxy-6-(4-methylpiperzin-1-yl)-1H-indole (intermediate 3 in WO95/06627) following a similar procedure to Example 2.

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm):8.27 (dd, 1H), 7.68 (s, 1H), 7.23-7.13 (m, 2H), 7.15 (dd, 1H), 6.75 (s, 1H), 4.15 (t, 2H), 3.85 (s, 3H), 3.22 (t, 2H), 3.13 (br s, 4H), 2.63 (br s, 4H), 2.36 (s, 3H).

Example 4

2,3-Dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole

To a stirred solution of triphosgene (84 mg, 0.28 mmole) in CH_2Cl_2 (10 ml) under argon, was added to a solution of 4-(pyridin-4-yl)naphth-1-ylamine (D2, 196 mg, 0.89 mmole) and NEt_3 (90 mg, 0.89 mmole) in CH_2Cl_2 (10 ml) dropwise over 30 min. After the addition was complete, the mixture was stirred at room temperature for 15 min, then a solution of 2,3-dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole (intermediate 3 in WO95/06627, 200 mg, 0.81 mmole) in CH_2Cl_2 (10 ml) was added. After 6h the mixture was washed with 10% Na_2CO_3(aq), dried (Na_2SO_4) and concentrated *in vacuo* giving a crude green oil, which was purified by chromatography on silica eluting with 2-5% MeOH/CH_2Cl_2. The title compound was obtained as a beige solid (292 mg, 73%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.73 (dd, 2H), 7.99 (dd, 1H), 7.91 (d, 1H), 7.88 (dd, 1H), 7.75 (s, 1H), 7.60-7.49 (m, 2H), 7.46 (d, 1H), 7.42 (dd, 2H), 6.81 (s, 1H), 6.77 (s, 1H), 4.27 (t, 2H), 3.85 (s, 3H), 3.28 (t, 2H), 3.11 (br s, 4H), 2.60 (br s, 4H), 2.34 (s, 3H).

Example 5

2,3-Dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1-[5-(4-pyridyl)naphth-1-ylaminocarbonyl]-1H-indole

The title compound was prepared from 5-(pyridin-4-yl)naphth-1-yl isocyanate (D4) and 2,3-dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole (intermediate 3 in WO95/06627) using a similar procedure to Example 2.

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.72 (d, 2H), 8.02 (d, 1H), 7.74 (s, 1H), 7.72 (d, 1H), 7.66 (d, 1H), 7.55 (t, 1H), 7.41-7.46 (m, 2H), 7.40 (d, 2H), 6.85 (s, 1H), 6.75 (s, 1H), 4.21 (t, 2H), 3.84 (s, 3H), 3.24 (t, 2H), 3.07 (brs, 4H), 2.56 (br s, 4H), 2.31 (s, 3H).

Example 6

1-[2,3-Dichloro-4-(pyridin-4-yl)phenylaminocarbonyl]-2,3-dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 2,3-dichloro-4-(pyridin-4-yl)aniline (D7) and 2,3-dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole (intermediate 3 in WO 95/06627) using a similar procedure to Example 4 as an orange/brown solid (54%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.67 (d, 2H), 8.41 (d, 1H), 7.70 (s, 1H), 7.36 (d, 2H), 7.27 (s, 1H), 7.26 (d, 1H), 6.76 (s, 1H), 4.18 (t, 2H), 3.85 (s, 3H), 3.24 (t, 2H), 3.18 (br s, 4H), 2.71 (br s, 4H), 2.41 (s, 3H).

Example 7

2,3-Dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1-(quinolin-5-ylaminocarbonyl)-1H-indole

The title compound was prepared from 5-aminoquinoline and 2,3-dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole (intermediate 3 in WO95/06627) using a similar procedure to Example 4.

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.92 (dd, 1H), 8.27 (dd, 1H), 7.99 (t, 1H), 7.69-7.71 (m, 3H), 7.41 (dd, 1H), 6.75 (s, 1H), 6.70 (s, 1H), 4.20 (t, 2H), 3.85 (s, 3H), 3.25 (t, 2H), 3.09 (br s, 4H), 2.59 (br s, 4H), 2.32 (s, 3H).

Example 8

2,3-Dihydro-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole

The title compound was prepared from 4-(pyridin-4-yl)naphth-1-ylamine (D2) and 2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D11) using a similar procedure to Example 4 as a beige solid (50%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.75-8.70 (m, 2H), 7.99 (d, 1H), 7.92-7.86 (m, 2H), 7.75 (d, 1H), 7.62-7.40 (m, 5H), 7.09 (d, 1H), 6.90 (s, 1H), 6.56 (dd, 1H), 4.26 (t, 2H), 3.28-3.17 (m, 6H), 2.55-2.50 (m, 4H), 2.32 (s, 3H).

Example 9

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole

The title compound was prepared from 4-(pyridin-4-yl)naphth-1-ylamine (D2) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 4 (38%). This was converted to its hydrochloride salt as a yellow solid from acetone.

^{1}H NMR (free base) (250 MHz, $CDCl_3$) δ (ppm): 8.73-8.67 (m, 2H), 8.00 (dd, 1H), 7.91-7.82 (m, 3H), 7.62-7.37 (m, 5H), 7.18 (s, 1H), 6.92 (s, 1H), 4.26 (t, 2H), 3.24 (t, 2H), 3.06 (br s, 4H), 2.56 (br s, 4H), 2.32 (s, 3H).

Example 10

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole

The title compound was prepared from 2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole (E8) and benzyltrimethylammonium tribromide using a similar procedure Description 14 as a beige solid (86%). This material was converted to its hydrochloride salt as a yellow solid from acetone.

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.76-8.70 (m, 2H), 8.00 (d, 1H), 7.91-7.82 (m, 3H), 7.62-7.34 (m, 6H), 6.93 (s, 1H), 4.26 (t, 2H), 3.24 (t, 2H), 3.05 (br s, 4H), 2.56 (br s, 4H), 2.32 (s, 3H).

Example 11

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)phenylaminocarbonyl]-1H-indole

The title compound was prepared from 4-(pyridin-4-yl)aniline (D5) and 5-bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D15) using a similar procedure to Example 4 as a white solid (24%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.52-8.45 (m, 2H), 8.00 (s, 1H), 7.71 (s, 1H), 7.60-7.45 (m, 4H), 7.37 (dd, 2H), 7.18 (s, 1H), 4.05 (t, 2H), 3.03 (t, 2H), 2.92 (br s, 4H), 2.45 (br s, 4H), 2.20 (s, 3H).

Example 12

5-Bromo-1-[3-chloro-4-(pyridin-4-yl)phenylaminocarbonyl]-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 3-chloro-4-(pyridin-4-yl)aniline (D6) and 5-bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D15) using a similar procedure to Example 4 as a white solid (13%).

^{1}H NMR (250 MHz, $CDCl_3$ + d^6DMSO) δ (ppm): 8.75 (d, 2H), 8.40 (s, 1H), 7.92 (s, 1H), 7.88 (d, 1H), 7.75 (dd, 1H), 7.52 (s, 1H), 7.42 (d, 2H), 7.33 (d, 1H), 4.27 (t, 2H), 3.25 (t, 2H), 2.97 (br s, 4H), 2.60 (br s, 4H), 2.35 (s, 3H).

Example 13

2,3-Dihydro-5-methyl-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole

The title compound was prepared from 4-(pyridin-4-yl)naphth-1-ylamine (D2) and 2,3-dihydro-5-methyl-6-(4-methylpiperazin-1-yl)-1H-indole (D17) using a similar procedure to Example 4 (52%). This material was converted to its hydrochloride salt as a yellow solid from acetone.

^{1}H NMR (free base) (250 MHz, $CDCl_3$) δ (ppm): 8.73-8.70 (m, 2H), 7.98 (d, 1H), 7.93-7.85 (m, 2H), 7.73 (s, 1H), 7.60-7.48 (m, 5H), 7.02 (s, 1H), 6.95 (s, 1H), 4.23 (t, 2H), 3.22 (t, 2H), 2.95-2.90 (m, 4H), 2.54 (br s, 4H), 2.31 (s, 3H), 2.26 (s, 3H).

Example 14

1-[3-Chloro-4-(pyridin-4-yl)phenylaminocarbonyl]-2,3-dihydro-5-methyl-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 3-chloro-4-(pyridin-4-yl)aniline (D6) and 2,3-dihydro-5-methyl-6-(4-methylpiperazin-1-yl)-1H-indole (D17) using a similar procedure to Example 4 as a white solid (67%).

^{1}H NMR (250 MHz, d^6DMSO) δ (ppm): 8.92 (s, 1H), 8.80 (d, 2H), 8.08 (d, 1H), 7.87-7.83 (m, 2H), 7.63 (d, 2H), 7.56 (d, 1H), 7.14 (s, 1H), 4.27 (t, 2H), 3.24 (t, 2H), 2.94 (br s, 4H), 2.65 (br s, 4H), 2.38 (s, 3H), 2.32 (s, 3H).

Example 15

2,3-Dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-5-vinyl-1H-indole

The title compound was prepared from 4-(pyridin-4-yl)naphth-1-ylamine (D2) and 2,3-dihydro-6-(4-methylpiperazin-1-yl)-5-vinyl-1H-indole (D19) using a similar procedure to Example 4 (50%). This material was converted to its hydrochloride salt as a yellow solid from ethyl acetate.

^{1}H NMR (free base) (250 MHz, $CDCl_3$) δ (ppm): 8.77-8.70 (m, 2H), 8.00 (d, 1H), 7.96-7.86 (m, 2H), 7.76 (s, 1H), 7.65-7.40 (m, 5H), 7.37 (s, 1H), 7.0 (dd, 1H), 6.92 (s, 1H), 5.60 (dd, 1H), 5.15 (dd, 1H), 4.28 (t, 2H), 3.29 (t, 2H), 3.05-2.95 (m, 4H), 2.55 (br s, 4H), 2.33 (s, 3H).

Example 16

2,3-Dihydro-5-ethyl-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole

The title compound was prepared from 4-(pyridin-4-yl)naphth-1-ylamine (D2) and 2,3-dihydro-5-ethyl-6-(4-methylpiperazin-1-yl)-1H-indole (D21) using a similar procedure to Example 4 as a beige solid (43%). This material was converted to its hydrochloride salt as a yellow solid from acetone.

^{1}H NMR (free base) (250 MHz, $CDCl_3$) δ (ppm): 8.74-8.70 (m, 2H), 8.03-7.87 (m, 3H), 7.77 (s, 1H), 7.60-7.38 (m, 5H), 7.09 (s, 1H), 6.92 (s, 1H), 4.26 (t, 2H), 3.26 (t, 2H), 2.98-2.92 (m, 4H), 2.66 (q, 2H), 2.61 (br s, 4H), 2.36 (s, 3H), 1.23 (t, 3H).

Example 17

1-[3-Chloro-4-(pyridin-4-yl)phenylaminocarbonyl]-2,3-dihydro-5-ethyl-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 3-chloro-4-(pyridin-4-yl)aniline (D6) and 2,3-dihydro-5-ethyl-6-(4-methylpiperazin-1-yl)-1H-indole (D21) using a similar procedure to Example 4 as a white solid (33%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.72-8.62 (m, 2H), 7.73-7.65 (m, 2H), 7.50-7.20 (m, 4H), 7.07 (s, 1H), 6.60 (s, 1H), 4.09 (t, 2H), 3.18 (t, 2H), 2.97-2.90 (m, 4H), 2.66 (q, 2H), 2.57 (br s, 4H), 2.35 (s, 3H), 1.22 (t, 3H).

Example 18

2,3-Dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-5-trifluoromethyl-1H-indole

The title compound was prepared from 4-(pyridin-4-yl)naphth-1-ylamine (D2) and 2,3-dihydro-6-(4-methylpiperazin-1-yl)-5-trifluoromethyl-1H-indole (D23) using a similar procedure to Example 4 as a beige solid (42%). This material was converted to its hydrochloride salt as a yellow solid from acetone.

^{1}H NMR (free base) (250 MHz, $CDCl_3$) δ (ppm): 8.77-8.71 (m, 2H), 8.07 (s, 1H), 8.01-7.85 (m, 3H), 7.63-7.39 (m, 6H), 6.94 (s, 1H), 4.33 (t, 2H), 3.32 (t, 2H), 3.05-2.96 (m, 4H), 2.64 (br s, 4H), 2.38 (s, 3H).

Example 19

1-[3-Chloro-4-(pyridin-4-yl)phenylaminocarbonyl]-2,3-dihydro-6-(4-methylpiperazin-1-yl)-5-trifluoromethyl-1H-indole

The title compound was prepared from 3-chloro-4-(pyridin-4-yl)aniline (D6) and 2,3-dihydro-6-(4-methylpiperazin-1-yl)-5-trifluoromethyl-1H-indole (D23) using a similar procedure to Example 4 as a beige solid (17%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.69-8.65 (m, 2H), 8.05 (s, 1H), 7.67 (d, 1H), 7.46 (dd, 1H), 7.44-7.37 (m, 3H), 7.31 (d, 1H), 6.59 (s, 1H), 4.16 (t, 2H), 3.27 (t, 2H), 3.00-2.94 (m, 4H), 2.55 (br s, 4H), 2.34 (s, 3H).

Example 20

2,3-Dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylacetyl]-1H-indole

To a stirred suspension of 4-(pyridin-4-yl)naphth-1-ylacetic acid (D24, 213 mg, 0.81 mmole) in CH_2Cl_2 (30 ml) was added oxalyl chloride (206 mg, 1.6 mmole) followed by DMF (1 drop). After 2h the solvents and excess oxalyl chloride were removed *in vacuo* to afford the acid chloride as a pale yellow solid. This was dissolved in CH_2Cl_2 (15 ml) and added portionwise over 10 min to a stirred solution of 2,3-dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole (intermediate 3 in WO 95/06627, 200 mg, 0.81 mmole) and NEt_3 (164 mg, 1.6 mmole) in CH_2Cl_2 (15 ml) at 0°C under argon. After 30 min at 0°C the mixture was stirred at room temperature for 5h, then washed with 10% Na_2CO_3 (aq), dried (Na_2SO_4) and concentrated *in vacuo*. The crude green/brown oil was purified

by chromatography on silica eluting with 2-5% MeCH/CH_2Cl_2 to afford the title compound as a yellow solid (340 mg, 85%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.72 (d, 2H), 8.02 (s, 1H), 8.02 (d, 1H), 7.87 (d, 1H), 7.37-7.60 (m, 6H), 6.74 (s, 1H), 4.26 (s, 2H), 4.25 (t, 2H), 3.85 (s, 3H), 3.22 (t, 2H), 3.08 (br s, 4H), 2.57 (br s, 4H), 2.32 (s, 3H).

Example 21

2,3-Dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1-[5-(pyridin-4-yl)naphth-1-ylacetyl]-1H-indole

The title compound was prepared from 5-(pyridin-4-yl)naphth-1-ylacetic acid (D25) and 2,3-dihyro-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole (intermediate 3 in WO 95/06627) using a similar procedure to Example 20.

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.72, (d, 2H), 8.03 (d, 1H), 8.02 (s, 1H), 7.78 (dd, 1H), 7.59 (t, 1H), 7.45-7.39 (m, 5H), 6.74 (s, 1H), 4.25 (s, 2H), 4.22 (t, 2H), 3.84 (s, 3H), 3.20 (t, 2H), 3.07 (br s, 4H), 2.57 (br s, 4H), 2.31 (s, 3H)

Example 22

2,3-Dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylacetyl]-1H-indole

The title compound was prepared from 4-(pyridin-4-yl)naphth-1-ylacetic acid (D24) and 2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D11) using a similar procedure to Example 20 as a beige solid from ethyl acetate (72%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.75-8.70 (m, 2H), 8.04-7.94 (m, 2H), 7.88 (d, 1H), 7.62-7.33 (m, 6H), 7.09 (d, 1H), 6.61 (dd, 1H), 4.26 (s, 2H), 4.25 (t, 2H), 3.25-3.13 (m, 6H), 2.55-2.47 (m, 4H), 2.30 (s, 3H).

Example 23

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylacetyl]-1H-indole

The title compound was prepared from 4-(pyridin-4-yl)naphth-1-ylacetic acid (D24) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 20 as a yellow oil (50%). This material was converted to its hydrochloride salt as a beige solid from ethyl acetate.

^{1}H NMR (free base) (250 MHz, $CDCl_3$) δ (ppm): 8.75-8.70 (m, 2H), 8.08 (s, 1H), 8.00 (d, 1H), 7.88 (d, 1H), 7.65-7.35 (m, 6H), 7.19 (s, 1H), 4.27 (t+s, 4H), 3.20 (t, 2H), 3.06 (br s, 4H), 2.57 (br s, 4H), 2.33 (s, 3H).

Example 24

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylacetyl]-1H-indole

The title compound was prepared from 2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylacetyl]-1H-indole (E22) and benzyltrimethylammonium tribromide using a similar procedure to Description 14 (62%). This material was converted to its hydrochloride salt as a white solid from ethyl acetate.

^{1}H NMR (free base) (250 MHz, $CDCl_3$) δ (ppm): 8.75-8.70 (m, 2H), 8.08 (s, 1H), 8.00 (d, 1H), 7.89 (d, 1H), 7.63-7.35 (m, 7H), 4.27 (t+s, 4H), 3.20 (t, 2H), 3.04 (br s, 4H), 2.56 (br s, 4H), 2.32 (s, 3H).

Example 25

2,3-Dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylacetyl]-5-vinyl-1H-indole

The title compound was prepared from 4-(pyridin-4-yl)naphth-1-ylacetic acid (D24) and 2,3-dihydro-6-(4-methylpiperazin-1-yl)-5-vinyl-1H-indole (D19) using a similar procedure to Example 20 (45%). This material was converted to its hydrochloride salt as a white solid from acetone/ethyl acetate.

^{1}H NMR (free base) (250 MHz, $CDCl_3$) δ (ppm): 8.75-8.68 (m, 2H), 8.05-7.96 (m, 2H), 7.88 (d, 1H), 7.65-7.30 (m, 7H), 7.00 (dd, 1H), 5.60 (dd, 1H), 5.15 (dd, 1H), 4.28 (s, 2H), 4.26 (t, 2H), 3.22 (t, 2H), 2.98-2.91 (m, 4H), 2.52 (br s, 4H), 2.31 (s, 3H).

Example 26

5-Bromo-2,3-dihydro-6-(1-methylpiperidin-4-yl)-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole

The title compound was prepared from 4-(pyridin-4-yl)naphth-1-ylamine (D2) and 5-bromo-2,3-dihydro-6-(1-methylpiperidin-4-yl)-1H-indole (D39) using a similar procedure to Example 4 (11%).

^{1}H NMR (250 MHz, d^{6}DMSO) δ(ppm): 8.95 (s, 1H), 8.78 (dd, 2H), 8.19 (dd, 1H), 7.93 (m, 1H), 7.85 (dd, 1H), 7.54-7.69 (m, 6H), 7.46 (s, 1H), 4.37 (t, 2H), 3.27 (t, 2H), 2.95 (br d, 2H), 2.82 (m, 1H), 2.27 (s, 3H), 2.10 (m, 2H), 1.65 (m, 4H).

Example 27

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[5-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole

The title compound was prepared from 5-(pyridin-4-yl)naphth-1-yl isocyanate (D4) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 2.

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.73 (d, 2H), 8.02 (d, 1H), 7.83 (s, 1H), 7.74 (d, 1H), 7.70 (d, 1H), 7.59 (t, 1H), 7.47 - 7.40 (m, 4H), 7.17 (s, 1H), 6.86 (s, 1H), 4.27 (t, 2H), 3.25 (t, 2H), 3.11 (br s, 4H), 2.66 (br s, 4H), 2.38 (s, 3H).

Example 28

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[5-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole

The title compound was prepared from 5-(pyridin-4-yl)naphth-1-yl isocyanate (D4) and 5-bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D15) using a similar procedure to Example 2.

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.73 (d, 2H), 8.02 (d, 1H), 7.84 (s, 1H), 7.75 (d, 1H), 7.72 (d, 1H), 7.59 (t, 1H), 7.50 - 7.44 (m, 2H), 7.41 (d, 2H), 7.37 (s, 1H), 6.78 (s, 1H), 4.27 (t, 2H), 3.26 (t, 2H), 2.97 (br s, 4H), 2.56 (br s, 4H), 2.32 (s, 3H).

Example 29

2,3-Dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1-(quinolin-6-ylaminocarbonyl)-1H-indole

The title compound was prepared from quinolin-6-yl isocyanate (D26) and 2,3-dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole (intermediate 3 in WO 95/06627) using a similar procedure to Example 2.

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.78 (dd, 1H), 8.19 (d, 1H), 8.13 (dd, 1H), 8.03 (d, 1H), 7.73 (s, 1H), 7.58 (dd, 1H), 7.37 (dd, 1H), 6.83 (s, 1H), 6.74 (s, 1H), 4.13 (t, 2H), 3.84 (s, 3H), 3.20 (t, 2H), 3.16 (br s, 4H), 2.66 (br s, 4H), 2.37 (s, 3H).

Example 30

1-[4-(*t*-Butoxycarbonylamino)phenylaminocarbonyl]-5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 4-(*t*-butoxycarbonylamino)aniline (D40) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 4 (29%).

^{1}H NMR (250MHz, d^{6}DMSO) δ(ppm): 9.25 (s, 1H), 8.45 (s, 1H), 7.78 (s, 1H), 7.40 (m, 4H), 7.22 (s, 1H), 4.12 (t, 2H), 3.11 (t, 2H), 2.89 (m, 4H), 2.50 (m, 4H), 2.25 (s, 3H), 1.48 (s, 9H).

Example 31

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-(quinolin-6-ylaminocarbonyl)-1H-indole

The title compound was prepared from quinolin-6-yl isocyanate (D26) and 5-bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D15) using a similar procedure to Example 2.

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.82 (dd, 1H), 8.17 (d, 1H), 8.13 (dd, 1H), 8.05 (d, 1H), 7.85 (s, 1H), 7.57 (dd, 1H), 7.39 (t, 1H), 7.36 (s, 1H), 6.62 (s, 1H), 4.16 (t, 2H), 3.22 (t, 2H), 3.12 (t, 4H), 2.63 (br s, 4H), 2.37 (s, 3H).

Example 32

6-Bromo-2,3-dihydro-7-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1,2,3,4-tetrahydroquinoline

The title compound was prepared from 4-(pyridin-4-yl)naphth-1-ylamine (D2) and 6-bromo-7-(4-methylpiperazin-1-yl)-1,2,3,4-tetrahydroquinoline (D33) using a similar procedure to Example 4.

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.72 (d, 2H), 8.07 (d, 1H), 7.86 (dd, 1H), 7.67 (dd, 1H),7.51 (s, 1H), 7.47 - 7.40 (m, 6H), 7.26 (s, 1H), 3.89 (t, 2H), 3.03 (t, 4H), 2.81 (t, 2H), 2.56 (t, 4H), 2.31 (s, 3H), 2.03 (quintet, 2H).

Example 33

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-(4-phenoxyphenylaminocarbonyl)-1H-indole

The title compound was prepared from 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) and 4-phenoxyphenyl isocyanate using a similar procedure to Example 2.

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 7.81 (s, 1H), 7.38 - 7.28 (m, 4H), 7.13 (s, 1H), 7.10 - 6.96 (m, 5H), 6.43 (s, 1H), 4.04 (t, 2H), 3.15 (t, 2H), 3.08 (br s, 4H), 2.58 (br s, 4H), 2.33 (s, 3H).

Example 34

5-Chloro-1-[4-(4-chlorophenoxy)phenylaminocarbonyl]-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) and 4-(4-chlorophenoxy)aniline using a similar procedure to Example 4.

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 7.81 (s, 1H), 7.38 (d, 2H), 7.26 (d, 2H), 7.14 (s, 1H), 6.98 (d, 2H), 6.91 (d, 2H), 6.41 (s, 1H), 4.08 (t, 2H), 3.18 (t, 2H), 3.09 (br s, 4H), 2.61 (br s, 4H), 2.35 (s, 3H).

Example 35

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-(quinolin-6-ylaminocarbonyl)-1H-indole

The title compound was prepared from quinolin-6-yl isocyanate (D26) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 2.

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.79 (dd, 1H), 8.18 (d, 1H), 8.13 (dd, 1H), 8.03 (d, 1H), 7.85 (s, 1H), 7.59 (dd, 1H), 7.38 (dd, 1H), 7.15 (s, 1H), 6.90 (s, 1H), 4.15 (t, 2H), 3.19 (t, 2H), 3.15 (br s, 4H), 2.67 (br s, 4H), 2.39 (s, 3H).

Example 36

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-(3-phenoxyphenylaminocarbonyl)-1H-indole

The title compound was prepared from 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) and 3-phenoxyaniline using a similar procedure to Example 4.

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 7.77 (s, 1H), 7.36 - 6.96 (m, 9H), 6.71 (ddd, 1H), 6.46 (s, 1H), 4.03 (t, 2H), 3.13 (t, 2H), 3.08 (br s, 4H), 2.60 (br s, 4H), 2.35 (s, 3H).

Example 37

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyrimidin-2-yl)phenylamino-carbonyl]-1H-indole

The title compound was prepared from 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) and 4-(pyrimidin-2-yl)phenyl isocyanate (D42) using a similar procedure to Example 2, giving a pale cream powder (69%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.78 (d, 2H), 8.40 (d, 2H), 7.83 (s, 1H), 7.60 (d, 2H), 7.15 (m, 2H), 6.56 (s, 1H), 4.12 (t, 2H), 3.18 (t, 2H), 3.11 (br s, 4H), 2.60 (br s, 4H), 2.35 (s, 3H).

Example 38

1-(3-Benzoylphenylaminocarbonyl)-5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 3-aminobenzophenone and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 4.

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 7.88 (m, 1H), 7.78 - 7.74 (m, 4H), 7.57 (d, 1H), 7.49 - 7.40 (m, 4H), 7.11 (s, 1H), 6.95 (s, 1H), 4.10 (t, 2H), 3.16 - 3.04 (m, 6H), 2.63 (br s, 4H), 2.37 (s, 3H).

Example 39

1-(4-Benzoylphenylaminocarbonyl)-5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 4-aminobenzophenone and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 4.

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 7.81 - 7.74 (m, 5H), 7.58 (m, 1H), 7.56 (d, 2H), 7.47 (t, 2H), 7.13 (s, 1H), 6.85 (s, 1H), 4.10 (t, 2H), 3.15 (t, 2H), 3.09 (br s, 4H), 2.59 (br s, 4H), 2.35 (s, 3H).

Example 40

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-(2-methylquinolin-6-ylaminocarbonyl)-1H-indole

The title compound was prepared from 6-amino-2-methylquinoline and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 4.

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.05 (d, 1H), 7.95 (d, 1H), 7.93 (d, 1H), 7.83 (s, 1H), 7.54 (dd, 1H), 7.22 (d, 1H), 7.12 (s, 1H), 6.75 (s, 1H), 4.07 (t, 2H), 3.16 - 3.09 (m, 6H), 2.70 (s, 3H), 2.61 (br s, 4H), 2.35 (s, 3H).

Example 41

5-Chloro-2,3-dihydro-1-[4-(fur-2-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 5-chloro-2,3-dihydro-1-(4-iodophenylaminocarbonyl)-6-(4-methylpiperazin-1-yl)-1H-indole (D43) and 2-furylboronic acid in a similar manner to Description 2, obtained as a pale buff powder (64%).

^{1}H NMR (250 MHz, d^6DMSO) δ (ppm): 8.68 (s, 1H), 7.82 (s, 1H), 7.73 (d, 1H), 7.76 (s,4H), 7.25 (s, 1H), 6.86 (d, 1H), 6.61 (dd, 1H), 4.18 (t, 2H), 3.15 (t, 2H), 2.95 (br s, 4H), 2.26 (s, 3H). 2 x CH_2 signals obscurred by DMSO signal.

Example 42

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(thien-2-yl)phenylaminocarbonyl]-1H-indole

The title compound was prepared from 5-chloro-2,3-dihydro-1-(4-iodophenylaminocarbonyl)-6-(4-methylpiperazin-1-yl)-1H-indole (D43) and 2-thienylboronic acid in a similar manner to Description 2, obtained as a cream powder (56%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 7.82 (s, 1H), 7.58 (d, 2H), 7.42 (d, 2H), 7.24 (d, 2H), 7.14 (s, 1H), 7.08 (m, 1H), 6.45 (s, 1H), 4.09 (t, 2H), 3.18 (t, 2H), 3.10 (br s, 4H), 2.60 (br s, 4H), 2.35 (s, 3H).

Example 43

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[5-(pyridin-4-yl)naphth-1-ylacetyl]-1H-indoline

The title compound was prepared from 5-(pyridin-4-yl)naphth-1-ylacetic acid (D25) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 20.

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.73 (dd, 2H), 8.07 (s, 1H), 8.01 (d, 1H), 7.79 (dd, 1H), 7.61 (dd, 1H), 7.45 - 7.41 (m, 5H), 7.19 (s, 1H), 4.27 (s, 2H), 4.26 (t, 2H), 3.19 (t, 2H), 3.05 (br s, 4H), 2.56 (br s, 4H), 2.32 (s, 3H).

Example 44

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[5-(pyridin-4-yl)naphth-1-ylacetyl]-1H-indole

The title compound was prepared from 5-(pyridin-4-yl)naphth-1-ylacetic acid (D25) and 5-bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D15) using a similar procedure to Example 20.

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.73 (d, 2H), 8.08 (s, 1H), 8.00 (d, 1H), 7.78 (dd, 1H), 7.60 (dd, 1H), 7.44 - 7.41 (m, 5H), 7.37 (s, 1H), 4.26 (s, 2H), 4.25 (t, 2H), 3.18 (t, 2H), 3.03 (br s, 4H), 2.56 (br s, 4H), 2.32 (s, 3H).

Example 45

5-Chloro-2,3-dihydro-1-[4-(1-methylpiperidin-4-yl)naphth-1-ylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 4-(1-methylpiperidin-4-yl)naphth-1-ylamine (D46) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 4.

^{1}H NMR (dihydrochloride salt) (250 MHz, d^{6}DMSO) δ (ppm): 11.06 (br s, 1H), 10.94 (br s, 1H), 8.82 (s, 1H), 8.27 (dd, 1H), 8.11 (dd, 1H), 7.78 (s, 1H), 7.63 (m, 2H), 7.54 (d, 1H), 7.42 (d, 1H), 7.33 (s, 1H), 4.30 (t, partially obscurred, 2H), 3.74 (m, 1H), 3.24 (t, 2H), 3.60 - 2.96 (m, 12H), 2.84 (s, 3H), 2.83 (s, 3H), 2.18 (m, 4H).

Example 46

5-Chloro-2,3-dihydro-1-[4-(2-methyloxazol-4-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 4-(4-aminophenyl)-2-methyloxazole (D47) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 4 as a pale yellow powder (67%).

^{1}H NMR (250 MHz, d^{6}DMSO) δ (ppm): 8.61 (s, 1H), 8.30 (s, 1H), 7.74 (s, 1H), 7.57 (dd, 4H), 7.21 (s, 1H), 4.13 (t, 2H), 3.08 (m, 6H), 2.75 (s, 3H), 2.38 (s, 3H). 2 x CH_2 signals obscurred by H_2O signal.

Example 47

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(2-methylpyridin-4-yl)phenylaminocarbonyl]-1H-indole

The title compound was prepared from 4-(2-methylpyridin-4-yl)aniline (D49) and 5-bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D15) using a similar procedure to Example 4 as a white solid (48%).

^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.52 (d, 1H), 7.83 (s, 1H), 7.64 - 7.52 (m, 4H), 7.38-7.33 (m, 2H), 7.29 (d, 1H), 6.54 (s, 1H), 4.11 (t, 2H), 3.19 (t, 2H), 3.09 (br s, 4H), 2.62 (br s, 4H + s, 3H), 2.35 (s, 3H).

Example 48

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(2-methylpyridin-4-yl)phenylaminocarbonyl]-1H-indole

The title compound was prepared from 4-(2-methylpyridin-4-yl)aniline (D49) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 4 as a beige solid (79%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 8.52(d, 1H), 7.82 (s, 1H), 7.62-7.50 (m, 4H), 7.34 (s, 1H), 7.28 (dd, 1H), 7.14 (s, 1H), 6.52 (s, 1H), 4.11 (t, 2H), 3.18 (t, 2H), 3.13-3.04 (m, 4H), 2.61 (s, 3H), 2.60 (br s, 4H), 2.34 (s, 3H).

Example 49

5-Chloro-2,3-dihydro-1-[4-(2,6-dimethylpyridin-4-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 4-(2,6-dimethylpyridin-4-yl)phenyl isocyanate (D62) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 2 as a white solid (55%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 7.82 (s, 1H), 7.60 - 7.50 (m, 4H), 7.16 - 7.11 (m, 3H), 6.63 (s, 1H), 4.07 (t, 2H), 3.15 (t, 2H), 3.09 (br s, 4H), 2.61 (br s, 4H), 2.57 (s, 6H), 2.35 (s, 3H).

Example 50

5-Bromo-2,3-dihydro-1-[4-(2,6-dimethylpyridin-4-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 4-(2,6-dimethylpyridin-4-yl)phenyl isocyanate (D62) and 5-bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D15) using a similar procedure to Example 2 as a white solid (36%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 7.83 (s, 1H), 7.61 - 7.51 (m, 4H), 7.34 (s, 1H), 7.16 (s, 2H), 6.54 (s, 1H), 4.11 (t, 2H), 3.19 (t, 2H), 3.09 (br s, 4H), 2.62 (br s, 4H), 2.58 (s, 6H), 2.35 (s, 3H).

Example 51

2,3-Dihydro-1-[4-(2,6-dimethylpyridin-4-yl)phenylaminocarbonyl]-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 4-(2,6-dimethylpyridin-4-yl)phenyl isocyanate (D62) and 2,3-dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole (intermediate 3 in WO 95/06627) using a similar procedure to Example 2 as a beige solid (28%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 7.70 (s, 1H), 7.61 - 7.50 (m, 4H), 7.16 (s, 2H), 6.74 (s, 1H), 6.51 (s, 1H), 4.11 (t, 2H), 3.84 (s, 3H), 3.20 (t, 2H), 3.13 (br s, 4H), 2.62 (br s, 4H), 2.58 (s, 6H), 2.35 (s, 3H).

Example 52

5-Chloro-2,3-dihydro-1-[4-(2,6-dimethylpyridin-3-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 4-(2,6-dimethylpyridin-3-yl)phenyl isocyanate (D63) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 2 as a white solid (21%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 7.83 (s, 1H), 7.48 (d, 2H), 7.40 (d, 1H), 7.28 (d, 2H), 7.16 (s, 1H), 7.04 (d, 1H), 6.49 (s, 1H), 4.11 (t, 2H), 3.20 (t, 2H), 3.10 (br s, 4H), 2.60 (br s, 4H), 2.57 (s, 3H), 2.49 (s, 3H), 2.35 (s, 3H).

Example 53

5-Bromo-2,3-dihydro-1-[4-(2,6-dimethylpyridin-3-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 4-(2,6-dimethylpyridin-3-yl)phenyl isocyanate (D63) and 5-bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D15) using a similar procedure to Example 2 as a white solid (44%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 7.84 (s, 1H), 7.50 (d, 2H), 7.41 (d, 1H), 7.35 (s, 1H), 7.29 (d, 2H), 7.06 (d, 1H), 6.48 (s, 1H), 4.12 (t, 2H), 3.21 (t, 2H), 3.09 (br s, 4H), 2.60 (br s, 4H), 2.57 (s, 3H), 2.49 (s, 3H), 2.35 (s, 3H).

Example 54

2,3-dihydro-1-[4-(2,6-dimethylpyridin-3-yl)phenylaminocarbonyl]-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 4-(2,6-dimethylpyridin-3-yl)phenyl isocyanate (D63) and 2,3-dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole (intermediate 3 in WO 95/06627) using a similar procedure to Example 2 as a beige solid (17%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 7.72 (s, 1H), 7.48 (d, 2H), 7.39 (d, 1H), 7.25 (d, 2H), 7.03 (d, 1H), 6.73 (s, 1H), 6.54 (s, 1H), 4.09 (t, 2H), 3.83 (s, 3H), 3.18 (t, 2H), 3.12 (br s, 4H), 2.60 (br s, 4H), 2.56 (s, 3H), 2.48 (s, 3H), 2.34 (s, 3H).

Example 55

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(5-methyl-1,2,4-oxadiazol-3-yl)phenylaminocarbonyl]-1H-indole

The title compound was prepared in an analogous manner to Example 4 from 4-(5-methyl-1,2,4-oxadiazol-3-yl)aniline (Ger. Offen DE 2046928) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13). The product was isolated as a pale cream powder (44%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 8.04 (d, 2H), 7.81 (s, 1H), 7.58(d, 2H), 7.15 (s, 1H), 6.53 (s, 1H), 4.10 (t, 2H), 3.19 (t, 2H), 3.10 (br s, 4H), 2.65 (s, 3H), 2.60 (br s, 4H), 2.35 (s, 3H).

Example 56

5-Chloro-2,3-dihydro-1-[4-(3-methyl-1,2,4-oxadiazol-5-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared in an analogous manner to Example 4 from 4-(3-methyl-1,2,4-oxadiazol-5-yl)aniline (J. Het. Chem. 1980, **17 (6)**, 1273-5) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13). The product was isolated as a cream powder (0.13g, 48%).

^{1}H NMR (250MHz, d^6DMSO) δ (ppm): 8.81 (s, 1H), 7.84 (d, 2H), 7.71 (d, 2H), 7.63 (s, 1H), 4.02 (t, 2H), 2.96 (t, 2H), 2.76 (br s, 4H), 2.34 (br s, 4H), 2.07 (s, 3H), 1.93 (s, 3H). NH proton not observed.

Example 57

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[3-(pyrimidin-2-yloxy)phenylaminocarbonyl]-1H-indole

The title compound was prepared in analogous manner to Example 4 from 3-(pyrimidin-2-yloxy)aniline (D71) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13). The product was isolated as a pale buff powder (32%).

^{1}H NMR (250MHz, d^6DMSO) δ (ppm): 8.55 (m, 3H), 7.63 (s, 1H), 7.35 (m, 2H), 7.26 - 7.10 (m, 3H), 6.75 (d, 1H), 4.02 (t, 2H), 2.99 (t, 2H), 2.78 (br s, 4H), 2.39 (br s, 4H), 2.10 (s, 3H).

Example 58

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-{4-[N-methyl-N-(pyrimidin-2-yl)amino]phenylaminocarbonyl}-1H-indole

The title compound was prepared in analogous manner to Example 4 from 4-[N-methyl-N-(pyrimidin-2-yl)amino]aniline (D73) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13). The product was isolated as a pale cream powder (54%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 8.34 (d, 2H), 7.80 (s, 1H), 7.46 (d, 2H), 7.29 (d, 2H), 7.15 (s, 1H), 6.56 (t, 1H), 6.42 (s, 1H), 4.08 (t, 2H), 3.50 (s, 3H), 3.18 (t, 2H), 3.09 (br s, 4H), 2.60 (br s, 4H), 2.35 (s, 3H).

Example 59

5-Bromo-2,3-dihydro-1-[4-(fur-2-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared in an analogous manner to Example 4 from 4-(fur-2-yl)aniline (Synthesis 1976, 1, 40) and 5-bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D15). The title compound was isolated as a cream powder (38%).

^{1}H NMR (250MHz, d^6DMSO) δ (ppm): 8.60 (s, 1H), 7.71 (s, 1H), 7.60 (d, 1H), 7.54 (s, 4H), 7.32 (s, 1H), 6.74 (d, 1H), 6.74 (d, 1H), 4.08 (t, 2H), 3.2 (br s, 4H), 3.04 (t, 2H), 2.97 (br s, 4H), 2.68 (s, 3H).

Example 60

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(thien-3-yl)phenylaminocarbonyl]-1H-indole

The title compound was prepared from 5-chloro-2,3-dihydro-1-(4-iodophenylaminocarbonyl)-6-(4-methylpiperazin-1-yl)-1H-indole (D43) and 3-thienylboronic acid in a similar manner to Description 2, obtained as a cream powder (31%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 7.83 (s, 1H), 7.57 (d, 2H), 7.45 (d, 2H), 7.38 (m, 3H), 7.15 (s, 1H), 6.42 (s, 1H), 4.10 (t, 2H), 3.18 (t, 2H), 3.10 (br s, 4H), 2.60 (br s, 4H), 2.35 (s, 3H).

Example 61

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(thiazol-2-yl)phenylaminocarbonyl]-1H-indole

The title compound was prepared from 4-(thiazol-2-yl)aniline (D52) and 5-bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D15) using a similar procedure to Example 4 (19%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 7.92 (d, 2H), 7.84 (d, 2H), 7.52 (d, 2H), 7.32 (d, 2H), 6.57 (s, 1H), 4.11 (t, 2H), 3.15 (t, 2H), 3.13 (br s, 4H), 2.69 (br s, 4H), 2.42 (s, 3H).

Example 62

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(thiazol-2-yl)phenylaminocarbonyl]-1H-indole

The title compound was prepared from 5-chloro-2,3-dihydro-1-(4-iodophenylaminocarbonyl)-6-(4-methylpiperazin-1-yl)-1H-indole (D43) and 2-bromothiazole using a similar procedure to D51 (8%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 7.93 (d, 2H), 7.83 (d, 2H), 7.58 (d, 2H), 7.28 (d, 1H), 7.14 (s, 1H), 6.57 (s, 1H), 4.10 (t, 2H), 3.17 (t, 2H), 3.11 (br s, 4H), 2.61 (br s, 4H), 2.35 (s, 3H).

Example 63

1-[4-(5-Acetylthien-2-yl)phenylaminocarbonyl]-5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 5-chloro-2,3-dihydro-1-(4-iodophenylaminocarbonyl)-6-(4-methylpiperazin-1-yl)-1H-indole (D43) and 5-acetylthien-2-ylboronic acid in a similar manner to Description 2, obtained a straw coloured solid (42%).

^{1}H NMR (250MHz, d^{6}DMSO) δ (ppm): 8.77 (s, 1H), 7.91 (d, 1H), 7.83 (s, 1H), 7.70 (m, 3H), 7.55 (d, 1H), 7.22 (s, 1H), 4.16 (t, 2H), 3.18 (t, 2H), 2.92 (br s, 4H), 2.51 (m, 7H), 2.23 (s, 3H). Urea NH not observed.

Example 64

1-(5-Bromonaphth-1-ylacetyl)-5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 5-bromonaphth-1-ylacetic acid (Bull. Soc. Chim. Fr. 1968, 7, 2957) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 20 as a light yellow foam (62%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 8.26 (d, 1H), 7.98 (s, 1H), 7.95 (d, 1H), 7.83 (d, 1H), 7.65 (t, 1H), 7.45 (d, 1H), 7.37 (t, 1H), 7.15 (s, 1H), 4.22 (s, 2H), 4.19 (t, 2H), 3.15 (t, 2H), 2.95 (br s, 4H), 2.48 (br s, 4H), 2.17 (s, 3H).

Example 65

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-(8-phenylquinolin-5-ylaminocarbonyl)-1H-indole

The title compound was prepared from 5-amino-8-phenylquinoline (D66) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 4, as a cream coloured solid (40%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 8.95 (dd, 1H) 8.29 (dd, 1H) 7.83 (s, 1H), 7.72 - 7.65 (m, 3H), 7.53 - 7.38 (m, 5H), 7.18 (s, 1H), 6.67 (s, 1H), 4.22 (t, 2H), 3.24 (t, 2H), 3.06 (br s, 4H), 2.56 (br s, 4H), 2.32 (s, 3H).

Example 66

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-(8-phenylquinolin-5-ylaminocarbonyl)-1H-indole

The title compound was prepared from 5-amino-8-phenylquinoline (D66) and 5-bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D15) using a similar procedure to Example 4, as a cream coloured solid (25%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 8.96 (dd, 1H), 8.31 (dd, 1H), 7.84 (s, 1H), 7.74 - 7.66 (m, 4H), 7.52 - 7.41 (m, 4H), 7.38 (s, 1H), 6.65 (s, 1H), 4.25 (t, 2H), 3.27 (t, 2H), 3.05 (br s, 4H), 2.57 (br s, 4H), 2.32 (s, 3H).

Example 67

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[2-(2-phenylethyl)quinolin-6-ylaminocarbonyl]-1H-indole

The title compound was prepared from 6-amino-2-(2-phenylethyl)quinoline (D69) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 4, as a white solid (77%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 8.09 (d, 1H), 8.01 (d, 1H), 7.99 (d, 1H), 7.85 (s, 1H), 7.56 (dd, 1H), 7.31 - 7.15 (m, 7H), 6.62 (s, 1H), 4.12 (t, 2H), 3.30 - 3.11 (m, 10H), 2.61 (br s, 4H), 2.35 (s, 3H).

Example 68

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[5-(1-methylpiperidin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole

The title compound was prepared from 5-(1-methylpiperidin-4-yl)naphth-1-ylamine (D77) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 4as a white solid (15%).

^{1}H NMR (250MHz,$CDCl_3$) δ(ppm):7.99 (d, 1H), 7.79 (m, 3H), 7.50 (m, 3H), 7.16 (s, 1H), 6.70 (s, 1H), 4.24 (t, 2H), 3.32 (m, 1H), 3.24 (t, 2H), 3.04 (br s, 4H), 2.56 (br s, 6H), 2.38 (s, 3H), 2.32 (s, 3H), 2.21 (m, 2H), 1.97 (m, 4H).

Example 69

5-Bromo-2,3-dihydro-1-[4-(isoquinolin-4-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 4-(isoquinolin-4-yl)phenyl isocyanate (D54) and 5-bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D15) using a similar procedure to Example 2, as a white solid (24%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 9.25 (s, 1H), 8.47 (s, 1H), 8.05 (d, 1H), 8.01 (d, 1H), 7.86 (s, 1H), 7.68 (m, 2H), 7.59 (d, 2H), 7.50 (d, 2H), 7.36 (s, 1H), 6.57 (s, 1H), 4.16 (t, 2H), 3.26 (t, 2H), 3.10 (br s, 4H), 2.61 (br s, 4H), 2.36 (s, 3H).

Example 70

5-Chloro-2,3-dihydro-1-[4-(isoquinolin-4-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 4-(isoquinolin-4-yl)phenyl isocyanate (D54) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 2, as a white solid (25%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 9.25 (s, 1H), 8.47 (s, 1H), 8.02 (d, 1H), 7.94 (d, 1H), 7.85 (s, 1H), 7.67 (m, 2H), 7.61 (d, 2H), 7.49 (d, 2H), 7.16 (s, 1H), 6.60 (s, 1H), 4.16 (t, 2H), 3.25 (t, 2H), 3.18 (br s, 4H), 2.61 (br s, 4H), 2.35 (s, 3H).

Example 71

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(quinolin-3-yl)phenylaminocarbonyl]-1H-indole

The title compound was prepared from 4-(quinolin-3-yl)phenyl isocyanate (D56) and 5-bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D15) using a similar procedure to Example 2, as an off white solid (6%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 9.17 (d, 1H), 8.27 (d, 1H), 8.13 (d, 1H), 7.85 (m, 2H), 7.62 (m, 6H), 7.34 (s, 1H), 6.57 (s, 1H), 4.14 (t, 2H), 3.20 (t, 2H), 3.17 (br s, 4H), 2.62 (br s, 4H), 2.37 (s, 3H).

Example 72

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(quinolin-3-yl)phenylaminocarbonyl]-1H-indole

The title compound was prepared from 4-(quinolin-3-yl)phenyl isocyanate (D56) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 2, as a light beige solid (10%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 9.17 (s, 1H), 8.27 (s, 1H), 8.13 (d, 1H), 7.87 (d, 1H), 7.84 (s, 1H), 7.73 (m, 3H), 7.60 (m, 3H), 7.16 (s, 1H), 6.54 (s, 1H), 4.14 (t, 2H), 3.21 (t, 2H), 3.12 (br s, 4H), 2.62 (br s, 4H), 2.36 (s, 3H).

Example 73

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[(2-methyl-1,2,3,4-tetrahydroisoquinolin-7-yl)aminocarbonyl]-1H-indole

The title compound was prepared from 7-amino-2-methyl-1,2,3,4-tetrahydroisoquinoline (D78) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 4 as a off-white solid (23%).

^{1}H NMR (250MHz,$CDCl_3$) δ(ppm): 7.80 (s, 1H), 7.10 (m, 4H), 6.36 (s, 1H), 4.04 (t, 2H), 3.55 (s, 2H), 3.15 (t, 2H), 3.09 (br s, 4H), 2.87 (m, 2H), 2.66 (m, 2H), 2.59 (br s, 4H), 2.44 (s, 3H), 2,34 (s, 3H).

Example 74

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[(2-methyl-1,2,3,4-tetrahydroisoquinolin-7-yl)aminocarbonyl]-1H-indole

The title compound was prepared from 7-amino-2-methyl-1,2,3,4-tetrahydroisoquinoline (D78) and 5-bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D15) using a similar procedure to Example 4 as an off-white solid (41%).

^{1}H NMR (250MHz,$CDCl_3$) δ(ppm): 7.80 (s, 1H), 7.32 (s, 1H), 7.09 (m, 3H), 6.35 (s, 1H), 4.05 (t, 2H), 3.55 (s, 2H), 3.16 (t, 2H), 3.07 (br s, 4H), 2.87 (m, 2H), 2.67 (m, 2H), 2.59 (br s, 4H), 2.44 (s, 3H), 2.34 (s, 3H).

Example 75

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(quinolin-8-yl)phenylaminocarbonyl]-1H-indole

The title compound was prepared from 4-(quinolin-8-yl)phenyl isocyanate (D58) and 5-bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D15) using a similar procedure to Example 2, as a white solid (52%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 8.94 (m, 1H), 8.20 (m, 1H), 7.84 (s, 1H), 7.82 (d, 1H), 7.62 (m, 6H), 7.41 (m, 1H), 7.36 (s, 1H), 6.53 (s, 1H), 4.12 (t, 2H), 3.19 (t, 2H), 3.10 (br s, 4H), 2.61 (br s, 4H), 2.35 (s, 3H).

Example 76

5-Chloro-6-(4-methylpiperazin-1-yl)-1-[4-(quinolin-8-yl)phenylaminocarbonyl]-1H-indole

The title compound was prepared from 4-(quinolin-8-yl)phenyl isocyanate (D58) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 2, as a white solid (71%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 8.93 (m, 1H), 8.20 (d, 1H), 7.80 (m, 2H), 7.57 (m, 6H), 7.41 (m, 1H), 7.15 (s, 1H), 6.53 (s, 1H), 4.12 (t, 2H), 3.19 (t, 2H), 3.12 (br s, 4H), 2.62 (br s, 4H), 2.37 (s, 3H).

Example 77

5-Chloro-2,3-dihydro-1-[4-(imidazol-1-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared in an analogous manner to Example 4 from 4-(imidazol-1-yl)aniline (J. Med. Chem. 1988, 31(11), 2136) and 5-chloro-2,3-

dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13). The product was isolated as a pale cream powder (42%).

^{1}H NMR (250MHz, d^{6}DMSO) δ (ppm): 8.70 (s, 1H), 8.20 (s, 1H), 7.81 (s, 1H), 7.72 (m, 3H), 7.57 (d, 2H), 7.25 (s, 1H), 7.12 (s, 1H), 4.21 (t, 2H), 3.15 (t, 2H), 2.94 (m, 4H), 2.52 (br s, 4H), 2.25 (s, 3H).

Example 78

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)phenylaminocarbonyl]-1H-indole

The title compound was prepared in an analogous manner to Description 2 from 5-chloro-2,3-dihydro-1-[4-iodophenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole (D43) and 4-pyridylboronic acid (J. Med Chem. 1997, **40(22)**, 3542). The product was isolated as a pale yellow solid (46%).

^{1}H NMR (250MHz, d^{6}DMSO) δ (ppm): 8.51 (s, 1H), 8.36 (d, 2H), 7.57 - 7.42 (m, 7H), 7.00 (s, 1H), 3.92 (t, 2H), 2.94 (t, 2H), 2.71 (m, 4H), 2.02 (s, 3H).
4H obscured by DMSO signal.

Example 79

2,3-Dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1-[(8-phenylquinolin-5-yl)aminocarbonyl]-1H-indole

The title compound was prepared from 5-amino-8-phenylquinoline (D66) and 2,3-dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole (intermediate 3 in WO 95/06627) using a similar procedure to Example 4, as a yellow/brown oil (20%). This was converted to the HCl salt as a yellow solid from acetone.

^{1}H NMR (free base) (250MHz, $CDCl_3$) δ (ppm): 8.95 (dd, 1H), 8.35 (dd, 1H), 7.77 - 7.65 (m, 4H), 7.52 - 7.37 (m, 5H), 6.79 (s, 1H), 6.76 (s, 1H), 4.25 (t, 2H), 3.85 (s, 3H), 3.27 (t, 2H), 3.14 (br s, 4H), 2.66 (br s, 4H), 2.37 (s, 3H).

Example 80

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[(8-phenylquinolin-4-yl)aminocarbonyl]-1H-indole

The title compound was prepared from 8-phenylquinolin-4-yl isocyanate (D86) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 2, as a yellow solid (75%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 8.86 (d, 1H), 8.15 (d, 1H), 7.85 (s, 1H), 7.77 - 7.38 (m, 9H), 7.19 (s, 1H), 4.27 (t, 2H), 3.25 (t, 2H), 3.12 (br s, 4H), 2.63 (br s, 4H), 2.37 (s, 3H).

Example 81

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[(8-phenylquinolin-4-yl)aminocarbonyl]-1H-indole

The title compound was prepared from 8-phenylquinolin-4-yl isocyanate (D86) and 5-bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D15) using a similar procedure to Example 2, as a yellow solid (75%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 8.87 (d, 1H), 8.16 (d, 1H), 7.85 (s, 1H), 7.78 - 7.39 (m, 9H), 7.28 (s, 1H), 4.29 (t, 2H), 3.27 (t, 2H), 3.11 (br s, 4H), 2.63 (br s, 4H), 2.37 (s, 3H).

Example 82

2,3-Dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1-[(8-phenylquinolin-4-yl)aminocarbonyl]-1H-indole

The title compound was prepared from 8-phenylquinolin-4-yl isocyanate (D86) and 2,3-dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole (intermediate 3 in WO 95/06627) using a similar procedure to Example 2, as a beige solid (73%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 8.86 (d, 1H), 8.19 (d, 1H), 7.79 - 7.38 (m, 9H), 7.33 (s, 1H), 6.78 (s, 1H), 4.28 (t, 2H), 3.86 (s, 3H), 3.27 (t, 2H), 3.14 (br s, 4H), 2.63 (br s, 4H), 2.36 (s, 3H).

Example 83

5-Chloro-1-[4-(2,6-dimethylpyridin-4-yl)-3-methylphenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 4-(2,6-dimethylpyridin-4-yl)-3-methylaniline (D88) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 4 as a pale yellow solid (41%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 7.82 (s, 1H), 7.36 (d, 1H), 7.31 (dd, 1H), 7.20-7.10 (m, 2H), 6.90 (s, 2H), 6.46 (s, 1H), 4.10 (t, 2H), 3.18 (t, 2H), 3.10 (br s, 4H), 2.60 (br s, 4H), 2.56 (s, 6H), 2.35 (s, 3H), 2.27 (s, 3H).

Example 84

5-Chloro-2,3-dihydro-1-[3-methyl-4-(6-methylpyridin-2-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 3-methyl-4-(6-methylpyridin-2-yl)aniline (D89) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 4 as a pale yellow gum (86%). This was converted to its hydrochloride salt as a pale yellow solid from acetone.

^{1}H NMR (free base) (250MHz, $CDCl_3$) δ (ppm): 7.83 (s, 1H), 7.62 (t, 1H), 7.40-7.28 (m, 3H), 7.20-7.14 (m, 2H), 7.09 (d, 1H), 6.42 (s, 1H), 4.10 (t, 2H), 3.18 (t, 2H), 3.10 (br s, 4H), 2.61 (br s, 7H), 2.36 (s, 3H), 2.35 (s, 3H).

Example 85

5-Bromo-2,3-dihydro-1-[3-methyl-4-(6-methylpyridin-2-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 3-methyl-4-(6-methylpyridin-2-yl)-3-methylaniline (D89) and 5-bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D15) using a similar procedure to Example 4 as a yellow foam (67%). This was converted to its hydrochloride salt as a beige solid from acetone.

^{1}H NMR (free base) (250MHz, $CDCl_3$) δ (ppm): 7.83 (s, 1H), 7.62 (t, 1H), 7.40-7.28 (m, 4H), 7.16 (d, 1H), 7.09 (d, 1H), 6.42 (s, 1H), 4.10 (t, 2H), 3.19 (t, 2H), 3.09 (br s, 4H), 2.61 (br s, 7H), 2.36 (s, 3H), 2.35 (s, 3H).

Example 86

2,3-Dihydro-5-methoxy-1-[3-methyl-4-(6-methylpyridin-2-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 3-methyl-4-(6-methylpyridin-2-yl)aniline (D89) and 2,3-dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole (intermediate 3 in WO 95/06627) using a similar procedure to Example 4 as a pale

yellow foam (84%). This was converted to its hydrochloride salt as a yellow solid from acetone.

^{1}H NMR (free base) (250MHz, $CDCl_3$) δ (ppm): 7.71 (s, 1H), 7.61 (t, 1H), 7.38-7,28 (m, 3H), 7.16 (d, 1H), 7.08 (d, 1H), 6.72 (s, 1H), 6.42 (s, 1H), 4.07 (t, 2H), 3.83 (s, 3H), 3.18 (t, 2H), 3.12 (br s, 4H), 2.60 (br s, 7H), 2.36 (s, 3H), 2.34 (s, 3H).

Example 87

5-Chloro-2,3-dihydro-1-[5-(6-methylpyridin-2-yl)naphth-1-ylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 5-(6-methylpyridin-2-yl)naphth-1-yl isocyanate (D92) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 4 as a pale yellow solid (59%). This was converted to its hydrochloride salt as a pale yellow solid from acetone.

^{1}H NMR (free base) (250MHz, $CDCl_3$) δ (ppm): 7.97 (dd, 1H), 7.87(d, 1H), 7.85 (s, 1H), 7.76-7.68 (m, 2H), 7.62-7.55 (m, 2H), 7.50-7.40 (m, 1H), 7.33 (d, 1H), 7.23 (d, 1H), 7.16 (s, 1H), 6.80 (s, 1H), 4.24 (t, 2H), 3.23 (t, 2H), 3.09 (br s, 4H), 2.67 (s, 3H), 2.61 (br s, 4H), 2.35 (s, 3H).

Example 88

2,3-Dihydro-5-methoxy-1-[5-(6-methylpyridin-2-yl)naphth-1-ylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 5-(6-methylpyridin-2-yl)naphth-1-yl isocyanate (D92) and 2,3-dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole (intermediate 3 in WO 95/06627) using a similar procedure to Example 4 as a pale yellow foam (55%). This was converted to its hydrochloride salt as a pale yellow solid from acetone.

^{1}H NMR (free base) (250MHz, $CDCl_3$) δ (ppm): 7.99 (dd, 1H), 7.85 (d, 1H), 7.82-7.68 (m, 3H), 7.62-7.55 (m, 2H), 7.50-7.41 (m, 1H), 7.34 (d, 1H), 7.21 (d, 1H), 6.76 (s, 2H), 4.24 (t, 2H), 3.85 (s, 3H), 3.26 (t, 2H), 3.15 (br s, 4H), 2.67 (br s, 7H), 2.38 (s, 3H).

Example 89

5-Chloro-2,3-dihydro-6-(4-ethylpiperazin-1-yl)-1-[4-pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole

The title compound was prepared from 4-(pyridin-4-yl)naphth-1-ylamine (D2) and 5-chloro-2,3-dihydro-6-(4-ethylpiperazin-1-yl)-1H-indole (D97) using a similar procedure to Example 4, as a beige solid (60%). The HCl salt was isolated as a yellow solid from acetone.

^{1}H NMR (free base) (250MHz, $CDCl_3$) δ (ppm): 8.74 (d, 2H), 8.00 (d, 1H), 7.91 (s, 1H), 7.91 - 7.86 (m, 2H), 7.61 - 7.42 (m, 5H), 7.19 (s, 1H), 6.81 (s, 1H), 4.30 (t, 2H), 3.28 (t, 2H), 3.11 (br s, 4H), 2.62 (br s, 4H), 2.48 (q, 2H), 1.11 (t, 3H).

Example 90

5-Chloro-2,3-dihydro-6-(4-ethylpiperazin-1-yl)-1-[5-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole

The title compound was prepared from 5-(pyridin-4-yl)naphth-1-ylamine (D74) and 5-chloro-2,3-dihydro-6-(4-ethylpiperazin-1-yl)-1H-indole (D97) using a similar procedure to Example 4, as a beige solid (68%). The HCl salt was isolated as a yellow solid from acetone.

^{1}H NMR (free base) (250MHz, $CDCl_3$) δ (ppm): 8.74 (d, 2H), 8.02 (d, 1H), 7.84 (s, 1H), 7.77 (d, 1H), 7.71 (d, 1H), 7.60 (t, 1H), 7.49 (t, 1H), 7.45 - 7.41 (m, 3H), 7.19 (s, 1H), 6.73 (s, 1H), 4.28 (t, 2H), 3.27 (t, 2H), 3.09 (br s, 4H), 2.60 (br s, 4H), 2.46 (q, 2H), 1.09 (t, 3H).

Example 91

5-Chloro-2,3-dihydro-6-(piperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole hydrochloride

A stirred solution of 6-[4-(*tert*-butyloxycarbonyl)piperazin-1-yl]-5-chloro-2,3-dihydro-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole (D100, 345mg, 0.59 mmole) in methanol (30ml) was treated with 1M HCl in ether (3ml). After 18h at room temperature additional HCl in ether (2.5ml) was added. After 24h the mixture was concentrated *in vacuo* and the residue solidified by trituration with acetone to afford the title compound as a yellow solid (260mg, 84%).

^{1}H NMR (250MHz, d^6DMSO) δ (ppm): 9.32 (s, 2H), 9.09 (s, 1H), 9.04 (d, 2H), 8.23 - 8.19 (m, 3H), 7.88 (dd, 1H), 7.77 - 7.59 (m, 5H), 7.30 (s, 1H), 4.37 (t, 2H), 3.24 - 3.18 (m, 6H), 3.10 (br s, 4H).

Example 92

5-Chloro-2,3-dihydro-6-(piperazin-1-yl)-1-[5-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole hydrochloride

The title compound was prepared from 6-[4-(*tert*-butyloxycarbonyl)piperazin-1-yl]-5-chloro-2,3-dihydro-1-[5-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole (D100) using a similar procedure to Example 91 as a beige solid (60%).

^{1}H NMR (250MHz, d^{6}DMSO) δ (ppm): 9.41 (s, 2H), 9.17 - 9.13 (m, 3H), 8.37 - 8.28 (m, 3H), 7.84 - 7.64 (m, 6H), 7.40 (s, 1H), 4.45 (t, 2H), 3.35 - 3.26 (m, 6H), 3.19 (br s, 4H).

Example 93

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridazin-3-yl)phenylaminocarbonyl]-1H-indole

The title compound was prepared from 4-(pyridizin-3-yl)benzoic acid (D102) using a similar procedure to Description 1 to form the isocyanate followed by addition of 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) to afford the urea as a pale yellow solid (7%).

^{1}H NMR (250MHz,$CDCl_3$) δ(ppm): 9.12 (dd, 1H), 8.06 (d, 2H), 7.82 (m, 2H), 7.61 (d, 2H), 7.51 (m, 1H), 7.14 (s, 1H), 6.63 (s, 1H), 4.12 (t, 2H), 3.19 (t, 2H), 3.11 (br s, 4H), 2.61 (br s, 4H), 2.36 (s, 3H).

Example 94

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridazin-3-yl)phenylaminocarbonyl]-1H-indole

The title compound was prepared from 4-(pyridazin-3-yl)benzoic acid (D102) using a similar procedure to Description 1 to form the isocyanate followed by addition of 5-bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D15) to afford the urea as a grey solid (3%).

^{1}H NMR (250MHz,$CDCl_3$) δ(ppm): 9.12 (dd, 1H), 8.08 (d, 2H), 7.83 (m, 2H), 7.62 (d, 2H), 7.52 (m, 1H), 7.34 (s, 1H), 6.60 (s, 1H), 4.13 (t, 2H), 3.20 (t, 2H), 3.10 (br s, 4H), 2.61 (br s, 4H), 2.36 (s, 3H).

Example 95

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyrazin-2-yl)phenylaminocarbonyl]-1H-indole

The title compound was prepared from 4-(pyrazin-2-yl)benzoic acid (D103) using a similar procedure to Description 1 to form the isocyanate followed by addition of 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) to afford the urea as a pale yellow solid (30%).

^{1}H NMR (250MHz,$CDCl_3$) δ(ppm): 9.01 (s, 1H), 8.61 (s, 1H), 8.47 (d, 1H), 8.02 (d, 2H), 7.83 (s, 1H), 7.61 (d, 2H), 7.16 (s, 1H), 6.55 (s, 1H), 4.13 (t, 2H), 3.20 (t, 2H), 3.11 (br s, 4H), 2.61 (br s, 4H), 2.36 (s, 3H).

Example 96

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyrazin-2-yl)phenylaminocarbonyl]-1H-indole

The title compound was prepared from 4-(pyrazin-2-yl)benzoic acid (D103) using a similar procedure to Description 1 to form the isocyanate followed by addition of 5-bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D15) to afford the urea as a pale yellow solid (49%).

^{1}H NMR (250MHz,$CDCl_3$) δ(ppm): 9.00 (s, 1H), 8.60 (s, 1H), 8.48 (s, 1H), 8.01 (d, 2H), 7.83 (s, 1H), 7.61 (d, 2H), 7.34 (s, 1H), 6.57 (s, 1H), 4.13 (t, 2H), 3.20 (t, 2H), 3.10 (br s, 4H), 2.62 (br s, 4H), 2.36 (s, 3H).

Example 97

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[(2-phenylpyridin-5-yl)aminocarbonyl]-1H-indole

The title compound was prepared from 6-phenylnicotinic acid (D104) using a similar procedure to Description 1 to form the isocyanate followed by addition of 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) to afford the urea as a white solid (48%).

^{1}H NMR (250MHz,d^6DMSO) δ(ppm): 8.87 (dd, 2H), 8.12 (m, 3H), 7.96 (d, 1H), 7.83 (s, 1H), 7.47 (m, 3H), 7.28 (s, 1H), 4.22 (t, 2H), 3.17 (t, 2H), 2.95 (br s, 4H), 2.54 (br s, obscured by DMSO peak, 4H), 2.26 (s, 3H).

Example 98

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[(2-phenylpyridin-5-yl)aminocarbonyl]-1H-indole

The title compound was prepared from 6-phenylnicotinic acid (D104) using a similar procedure to Description 1 to form the isocyanate followed by addition of 5-bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D15) to afford the urea as an off white solid (46%).

^{1}H NMR (250MHz,d^{6}DMSO) δ(ppm): 8.86 (dd, 2H), 8.12 (m, 3H), 8.09 (d, 1H), 7.83 (s, 1H), 7.47 (m, 4H), 4.22 (t, 2H), 3.18 (t, 2H), 2.94 (br s, 4H), 2.53 (br s, obscured by DMSO peak, 4H), 2.26 (s, 3H).

Example 99

5-Chloro-2,3-dihydro-1-[4-(6-methylpyridazin-3-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 4-(6-methylpyridazin-3-yl)benzoic acid (D105) using a similar procedure to Description 1 to form the isocyanate followed by addition of 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) to afford the urea as a buff solid (23%).

^{1}H NMR (250MHz,$CDCl_3$) δ(ppm): 8.03 (d, 2H), 7.83 (s, 1H), 7.71 (d, 1H), 7.58 (d, 2H), 7.35 (d, 1H), 7.14 (s, 1H), 6.59 (s, 1H), 4.11 (t, 2H), 3.18 (t, 2H), 3.11 (br s, 4H), 2.74 (s, 3H), 2.60 (br s, 4H), 2.36 (s, 3H).

Example 100

5-Bromo-2,3-dihydro-1-[4-(6-methylpyridazin-3-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 4-(6-methylpyridazin-3-yl)benzoic acid (D105) using a similar procedure to Description 1 to form the isocyanate followed by addition of 5-bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D15) to afford the urea as a buff solid (28%).

^{1}H NMR (250MHz,$CDCl_3$) δ(ppm): 8.05 (d, 2H), 7.84 (s, 1H), 7.72 (d, 1H), 7.60 (d, 2H), 7.35 (m, 2H), 6.57 (s, 1H), 4.13 (t, 2H), 3.20 (t, 2H), 3.10 (br s, 4H), 2.75 (s, 3H), 2.62 (br s, 4H), 2.36 (s, 3H).

Example 101

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-3-yl)phenylaminocarbonyl]-1H-indole

The title compound was prepared from 5-chloro-2,3-dihydro-1-(4-iodophenylaminocarbonyl)-6-(4-methylpiperazin-1-yl)-1H-indole (D43) and 3-pyridylboronic acid (Chem. Pharm. Bull, 1983, **31(12)**, 4573) in a similar manner to Description 2, obtained as a pale cream powder (19%).

^{1}H NMR (250 MHz, d^{6}DMSO) δ (ppm): 8.81 (s, 1H), 8.61 (s, 1H), 8.45 (d, 1H), 7.96 (d, 1H), 7.7 (s, 1H), 7.62 (m, 4H), 7.38 (m, 1H), 7.14 (s, 1H), 4.08 (t, 2H), 3.04 (t, 2H), 2.83 (br s, 4H), 2.15 (s, 3H). 2xCH_2 signals obscured by DMSO signal.

Example 102

5-Chloro-2,3-dihydro-1-[4-(5-methyloxazol-2-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) and 4-(5-methyloxazol-2-yl)aniline (D107) using a similar procedure to Example 4, obtained as a pale cream powder (63%).

^{1}H NMR (250 MHz, d^{6}DMSO) δ (ppm): 8.78 (s, 1H), 7.72 (m, 5H), 7.20 (s, 1H), 6.90 (s, 1H), 4.14 (t, 2H), 3.08 (t, 2H), 2.96 (br s, 4H), 2.72 (br s, 4H), 2.38 (s, 3H), 2.33 (s, 3H).

Example 103

2,3-Dihydro-5-methoxy-1-[4-(5-methyloxazol-2-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 2,3-dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole (Intermediate 3 in WO 95/06627) and 4-(5-methyloxazol-2-yl)aniline (D107) using a similar procedure to Example 4, obtained as a pale cream powder (44%).

^{1}H NMR (250 MHz, d^{6}DMSO) δ (ppm): 8.80 (s, 1H), 7.97 (d, 2H), 7.86 (d, 2H), 7.77 (s, 1H), 7.08 (s, 1H), 7.00 (s, 1H), 4.27 (t, 2H), 3.89 (s, 3H), 3.25 (t, 2H), 3.07 (br s, 4H), 2.61 (br s, 4H), 2.52 (s, 3H), 2.37 (s, 3H).

Example 104

5-Bromo-2,3-dihydro-1-[4-(5-methyloxazol-2-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 5-bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D15) and 4-(5-methyloxazol-2-yl)aniline (D107) using a similar procedure to Example 4, obtained as a pale cream powder (23%).

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 7.94 (d, 2H), 7.82 (s, 1H), 7.52 (d, 2H), 7.33 (s, 1H), 6.81 (s, 1H), 6.58 (d, 1H), 4.11 (t, 2H), 3.15 (m, 6H), 2.69 (br s, 4H), 2.42 (s, 3H), 2.39 (s, 3H).

Example 105

5-Chloro-2,3-dihydro-1-[4-(1-methylpyrazol-4-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 4-(1-methylpyrazol-4-yl)benzoic acid (WO 97/43262) using a similar procedure to Description 1 to form the isocyanate followed by addition of 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) to afford the urea as an off white solid (18%).

^{1}H NMR (250MHz,$CDCl_3$) δ(ppm): 7.82 (s, 1H), 7.72 (s, 1H), 7.55 (s, 1H), 7.41 (s, 4H), 7.13 (s, 1H), 6.44 (s, 1H), 4.07 (t, 2H), 3.93 (s, 3H), 3.16 (t, 2H), 3.10 (br s, 4H), 2.60 (br s, 4H), 2.35 (s, 3H).

Example 106

5-Bromo-2,3-dihydro-1-[4-(1-methylpyrazol-4-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 4-(1-methylpyrazol-4-yl)benzoic acid (WO 97/43262) using a similar procedure to Description 1 to form the isocyanate followed by addition of 5-bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D15) to afford the urea as a buff solid (30%).

^{1}H NMR (250MHz,$CDCl_3$) δ(ppm): 7.83 (s, 1H), 7.71 (s, 1H), 7.54 (s, 1H), 7.40 (s, 4H), 7.31 (s, 1H), 6.46 (s, 1H), 4.05 (t, 2H), 3.93 (s, 3H), 3.15 (t, 2H), 3.08 (br s, 4H), 2.60 (br s, 4H), 2.35 (s, 3H).

Example 107

5-Chloro-1-[4'-cyano-3'-methylbiphenyl-4-aminocarbonyl]-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 4-(4-cyano-3-methylphenyl)benzoic acid (D106) using a similar procedure to Description 1 to form the isocyanate followed by addition of 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) to afford the urea as a pale yellow solid (39%).

^{1}H NMR (250MHz,$CDCl_3$) δ(ppm): 7.82 (s, 1H), 7.64 (d, 1H), 7.44-7.55 (m, 6H), 7.15 (s, 1H), 6.52 (s, 1H), 4.11 (t, 2H), 3.19 (t, 2H), 3.10 (br s, 4H), 2.60 (br s, 7H), 2.35 (s, 3H).

Example 108

5-Bromo-1-[4'-cyano-3'-methylbiphenyl-4-aminocarbonyl]-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 4-(4-cyano-3-methylphenyl)benzoic acid (D106) using a similar procedure to Description 1 to form the isocyanate followed by addition of 5-bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D15) to afford the urea as a buff solid (28%).

^{1}H NMR (250MHz,$CDCl_3$) δ(ppm): 7.83 (s, 1H), 7.64 (d, 1H), 7.42-7.55 (m, 6H), 7.33 (s, 1H), 6.54 (s, 1H), 4.10 (t, 2H), 3.18 (t, 2H), 3.08 (br s, 4H), 2.60 (br s, 7H), 2.35 (s, 3H).

Example 109

5-Chloro-2,3-dihydro-1-[4-(2-methylpyridin-5-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 4-(2-methylpyridin-5-yl)benzoic acid (WO 97/43262) using a similar procedure to Description 1 to form the isocyanate followed by addition of 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) to afford the urea as a buff solid (2%).

^{1}H NMR (250MHz,$CDCl_3$) δ(ppm): 8.68 (d, 1H), 7.82 (s, 1H), 7.74 (dd, 1H), 7.53 (s, 4H), 7.21 (d, 1H), 7.14 (s, 1H), 6.50 (s, 1H), 4.11 (t, 2H), 3.18 (t, 2H), 3.11 (br s, 4H), 2.59 (br s, 7H), 2.36 (s, 3H).

Example 110

5-Bromo-2,3-dihydro-1-[4-(2-methylpyridin-5-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 4-(2-methylpyridin-5-yl)benzoic acid (WO 97/43262) using a similar procedure to Description 1 to form the isocyanate followed by addition of 5-bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D15) to afford the urea as a buff solid (10%).

^{1}H NMR (250MHz,d^{6}DMSO) δ(ppm): 8.79 (d, 1H), 8.73 (s, 1H), 7.99 (dd, 1H), 7.84 (s, 1H), 7.71 (q, 4H), 7.43 (s, 1H), 7.36 (d, 1H), 4.21 (t, 2H), 3.17 (t, 2H), 2.96 (br s, 4H), 2.54 (br s, obscured by DMSO peak, 7H), 2.31 (s, 3H).

Example 111

5-Chloro-2,3-dihydro-1-[5-(3-methyl-1,2,4-oxadiazol-5-yl)naphth-1-ylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) and 5-(3-methyl-1,2,4-oxadiazol-5-yl)naphth-1-ylamine (D111) using a similar procedure to Example 4. The title compound was converted to the hydrochloride salt as a pale buff powder (59%).

^{1}H NMR (HCl salt) (250MHz, d^{6}DMSO) δ (ppm): 10.82 (s, 1H), 9.03 (s, 1H), 8.92 (d, 1H), 8.42 (m, 2H), 7.78 - 7.65 (m, 4H), 7.31 (s, 1H), 4.34 (t, 2H), 3.48 - 2.94 (m, 10H), 2.80 (d, 3H), 2.54 (s, 3H).

Example 112

2,3-Dihydro-5-methoxy-1-[5-(3-methyl-1,2,4-oxadiazol-5-yl)naphth-1-ylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 2,3-dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole (intermediate 3 in WO 95/06627) and 5-(3-methyl-1,2,4-oxadiazol-5-yl)naphth-1-ylamine (D111) in a similar procedure to Example 4. The title compound was converted to the hydrochloride salt as colourless powder (68%).

^{1}H NMR (HCl salt) (250MHz, d^{6}DMSO) δ (ppm): 10.87 (s, 1H), 8,92 (s, 1H), 8,87 (d, 1H), 8.41 - 8.33 (m, 2H), 7.78 - 7.65 (m, 3H), 7.60 (s, 1H), 6.94 (s, 1H), 4.30 (t, 2H), 3.77 (s, 3H), 3.40 (m, 4H), 3.20 (m, 4H), 2.89 (t, 2H), 2.75 (d, 3H), 2.53 (s, 3H).

Example 113

5-Bromo-2,3-dihydro-1-[5-(3-methyl-1,2,4-oxadiazol-5-yl)naphth-1-ylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 5-bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-indole (D15) and 5-(3-methyl-1,2,4-oxadiazol-5-yl)naphth-1-ylamine (D111) in a similar procedure to Example 4. The title compound was converted to the hydrochloride salt as a pale buff powder (36%).

^{1}H NMR (HCl salt) (250MHz, d^{6}DMSO) δ (ppm): 10.75 (s, 1H), 9.07 (s, 1H), 8.92 (d, 1H), 8.39 (dd, 2H), 7.80 - 7.65 (m, 4H), 7.46 (s, 1H), 4.34 (t, 2H), 3.36 - 2.93 (m, 6H), 2.81 (d, 3H), 2.61 (s, 3H). 2xCH_2 signals obscurred by H_2O signal.

Example 114

5-Chloro-2,3-dihydro-1-[5-(5-methyloxazol-2-yl)naphth-1-ylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) and 5-(5-methyloxazol-2-yl)naphth-1-ylamine (D114) in a similar procedure to Example 4, converted to the hydrochloride salt as a pale yellow power (41%).

^{1}H NMR (HCl salt) (250MHz, d^{6}DMSO) δ (ppm): 10.94 (s, 1H), 9.16 (d, 1H), 8.96 (s, 1H), 8.18 (dd, 2H), 7.75 (s, 1H), 7.70 - 7.59 (m, 3H), 7.30 (s, 1H), 7.16 (s, 1H), 4.34 (t, 2H), 3.47 (t, 2H), 3.37 - 2.95 (m, 8H), 2.78 (d, 3H). CH_3 signal obscurred by DMSO signal.

Example 115

2,3-Dihydro-5-methoxy-1-[5-(5-methyloxazol-2-yl)naphth-1-ylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 2,3-dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole (intermediate 3 in WO 95/06627) and 5-(5-methyloxazol-2-yl)naphth-1-ylamine (D114) in a similar procedure to Example 4, obtained as the hydrochloride salt as a pale yellow powder (56%).

^{1}H NMR (HCl salt) (250MHz, d^{6}DMSO) δ (ppm): 10.95 (s, 1H), 9.14 (d. 1H), 8.79 (s, 1H), 8.17 (dd, 2H), 7.69 - 7.58 (m, 4H), 7.17 (s, 1H), 6.94 (s, 1H), 4.29 (t, 2H), 3.77 (s, 3H), 3.38 (m, 4H), 3.16 (m, 4H), 2.95 (t, 2H), 2.77 (d, 3H), 2.51 (s, 3H).

Example 116

5-Bromo-2,3-dihydro-1-[3-methyl-4-(pyrimidin-2-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 3-methyl-4-(pyrimidin-2-yl)aniline (D115) and 5-bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D15) using a similar procedure to Example 4 as a beige foam (34%). This foam was converted to its hydrochloride salt as a yellow solid from acetone.

^{1}H NMR (HCl salt) (250MHz, d^{6}DMSO) δ (ppm): 10.50 (br s, 1H), 8.90 (d, 2H), 8.75 (s, 1H), 7.84 (m, 2H), 7.60 (m, 2H), 7.43 (m, 2H), 4.20 (t, 2H), 3.54 (d, 1H), 3.33 (d, 1H), 3.10 (m, 6H), 2.85 (d, 3H), 2.54 (s, 3H).

Example 117

2,3-dihydro-5-methoxy-1-[3-methyl-4-(pyrimidin-2-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 3-methyl-4-(pyrimidin-2-yl)aniline (D115) and 2,3-dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole (intermediate 3 in WO 95/06627) using a similar procedure to Example 4 as a beige foam (32%). This foam was converted to its hydrochloride salt as a yellow-brown solid from acetone.

^{1}H NMR (HCl salt) (250MHz, d^{6}DMSO) δ (ppm): 10.45 (br s, 1H), 8.90 (d, 2H), 8.59 (s, 1H), 7.83 (d, 1H), 7.67 (s, 1H), 7.60 (m, 2H), 7.40 (t, 1H), 6.92 (s, 1H), 4.15 (t, 2H), 3.77 (s, 3H), 3.45 (m, 4H), 3.17 (m, 4H), 2.96 (t, 2H), 2.82 (d, 3H), 2.54 (s, 3H).

Example 118

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[3-methyl-4-(pyrimidin-2-yl)phenylaminocarbonyl]-1H-indole

The title compound wa prepared from 3-methyl-4-(pyrimidin-2-yl)aniline (D115) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 4 as a beige foam (47%). This foam was converted to its hydrochloride salt as a yellow solid from acetone.

^{1}H NMR (HCl salt) (250MHz, d^{6}DMSO) δ (ppm): 10.50 (br s, 1H), 8.90 (d, 2H), 8.71 (s, 1H), 7.84 (d, 1H), 7.82 (s, 1H), 7.60 (m, 2H), 7.41 (t, 1H), 7.29 (s, 1H), 4.20 (t, 2H), 3.53 (d, 2H), 3.37 (d, 2H), 3.14 (m, 6H), 2.86 (d, 3H), 2.54 (s, 3H).

Example 119

5-Bromo-2,3-dihydro-1-[3-methyl-4-(pyrimidin-5-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 3-methyl-4-(pyrimidin-5-yl)aniline (D116) and 5-bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D15) using a similar procedure to Example 4 as a foam (82%). This foam was converted to its hydrochloride salt as an off white solid from acetone.

^{1}H NMR (HCl salt) (250MHz, d^{6}DMSO) δ (ppm): 10.65 (br s, 1H), 9.18 (s, 1H), 8.86 (s, 2H), 8.73 (s, 1H), 7.82 (s, 1H), 7.62 (s, 1H), 7.55 (dd, 1H), 7.45 (s, 1H), 7.25 (d, 1H), 4.19 (t, 2H), 3.54-2.98 (m, 10H), 2.85 (d, 3H), 2.28 (s, 3H).

Example 120

5-Chloro-2,3-dihydro-1-[3-methyl-4-(pyrimidin-5-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 3-methyl-4-(pyrimidin-5-yl)aniline (D116) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 4 as foam (84%). This foam was converted to its hydrochloride salt as an off white solid from acetone.

^{1}H NMR (HCl salt) (250MHz, d^{6}DMSO) δ (ppm): 10.67 (br s, 1H), 9.18 (s, 1H), 8.86 (s, 2H), 8.73 (s, 1H), 7.82 (s, 1H), 7.58 (s, 1H), 7.55 (dd, 1H), 7.27 (m, 2H), 4.19 (t, 2H), 3.53-3.00 (m, 10H), 2.84 (d, 3H), 2.28 (s, 3H).

Example 121

2,3-Dihydro-5-methoxy-1-[3-methyl-4-(pyrimidin-5-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 3-methyl-4-(pyrimidin-5-yl)aniline (D116) and 2,3-dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole (intermediate 3 in WO 95/06627) using a similar procedure to Example 4 as a foam (97%). This foam was converted to its hydrochloride salt as an off white solid from acetone.

^{1}H NMR (HCl salt) (250MHz, d^{6}DMSO) δ (ppm): 10.74 (br s, 1H), 9.18 (s, 1H), 8.88 (s, 2H), 8.59 (s, 1H), 7.60 (m, 3H), 7.22 (d, 1H), 6.92 (s, 1H), 4.15 (t, 2H), 3.77 (s, 3H), 3.45 (m, 4H), 3.10 (m, 4H), 2.98 (t, 2H), 2.81 (d, 3H), 2.28 (s, 3H).

Example 122

5-Bromo-2,3-dihydro-1-[4-(2,6-dimethylpyridin-4-yl)-3-methylphenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 4-(2,6-dimethylpyridin-4-yl)-3-methylaniline (D88) and 5-bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D15) using a similar procedure to Example 4 as a pale yellow foam (89%). This was converted to its hydrochloride salt as a pale yellow solid from acetone.

^{1}H NMR (free base) (250MHz, $CDCl_3$) δ (ppm): 7.83 (s, 1H), 7.38-7.27 (m, 3H), 7.14 (d, 1H), 6.90 (s, 2H), 6.47 (s, 1H), 4.11 (t, 2H), 3.19 (t, 2H), 3.08 (br m, 4H), 2.60 (br m, 4H), 2.56 (s, 6H), 2.35 (s, 3H), 2.27 (s, 3H).

Example 123

2,3-Dihydro-5-methoxy-1-[4-(2,6-dimethylpyridin-4-yl)-3-methylphenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 4-(2,6-dimethylpyridin-4-yl)-3-methylaniline (D88) and 2,3-dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole (intermediate 3 in WO 95/06627) using a similar procedure to Example 4 as a pale yellow foam (95%). This was converted to its hydrochloride salt as a yellow solid from acetone.

^{1}H NMR (free base) (250MHz, $CDCl_3$) δ (ppm): 7.70 (s, 1H), 7.37 (d, 1H), 7.30 (dd, 1H), 7.14 (d, 1H), 6.90 (s, 2H), 6.73 (s, 1H), 6.42 (s, 1H), 4.09 (t, 2H), 3.84 (s, 3H), 3.20 (t, 2H), 3.12 (br, s, 4H), 2.61 (br s, 4H), 2.56 (s, 6H), 2.34 (s, 3H), 2.27 (s, 3H).

Example 124

5-Chloro-2,3-dihydro-1-[5-(2,6-dimethylpyridin-4-yl)naphth-1-ylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 5-(2,6-dimethylpyridin-4-yl)naphth-1-yl isocyanate (D119) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 4 as a white foam (83%). This was converted to its hydrochloride salt as a white solid from acetone.

^{1}H NMR (free base) (250MHz, $CDCl_3$) δ (ppm): 7.98 (d, 1H), 7.83 (s, 1H), 7.77-7.69 (m, 2H), 7.60-7.38 (m, 3H), 7.17 (s, 1H), 7.07 (s, 2H), 6.75 (s, 1H), 4.25 (t, 2H), 3.24 (t, 2H), 3.06 (br m, 4H), 2.62 (s, 6H), 2.56 (br m, 4H), 2.32 (s, 3H).

Example 125

5-Bromo-2,3-dihydro-1-[5-(2,6-dimethylpyridin-4-yl)naphth-1-ylaminocarbonyl]-6-(4-methylpiperazin-1-yl)indoline

The title compound was prepared from 5-(2,6-dimethyl-4-pyridyl)-1-naphthyl isocyanate (D119) and 5-bromo-6-(4-methylpiperazin-1-yl)indoline (D15) using a similar procedure to Example 4 as a white foam (64%). This was converted to its hydrochloride salt as a white solid from acetone.

^{1}H NMR (free base) (250MHz, $CDCl_3$) δ (ppm): 7.98 (d, 1H), 7.84 (s, 1H), 7.78-7.68 (m, 2H), 7.60-7.38 (m, 3H), 7.36 (s, 1H), 7.08 (s, 2H), 6.75 (s, 1H), 4.25 (t, 2H), 3.25 (t, 2H), 3.05 (br m, 4H), 2.62 (s, 6H), 2.57 (br m, 4H), 2.32 (s, 3H).

Example 126

1-[5-(2,6-Dimethyl-4-pyridyl)-1-naphthylaminocarbonyl]-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 5-(2,6-dimethylpyridin-4-yl)naphth-1-yl isocyanate (D119) and 2,3-dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole (intermediate 3 in WO 95/06627) using a similar procedure to Example 4 as a colourless oil (88%). This was converted to its hydrochloride salt as a pale yellow solid from acetone.

^{1}H NMR (free base) (250MHz, $CDCl_3$) δ (ppm): 7.99 (d, 1H), 7.78 (d, 1H), 7.74 (s, 1H), 7.68 (d, 1H), 7.60-7.36 (m, 3H), 7.08 (s, 2H), 6.76 (s, 1H), 6.72 (s, 1H), 4.24 (t, 2H), 3.85 (s, 3H), 3.27 (t, 2H), 3.09 (br s, 4H), 2.62 (s, 6H), 2.57 (br m, 4H), 2.32 (s, 3H).

Example 127

2,3-Dihydro-1-[4-(2,6-dimethylpyridin-3-yl)-3-methylphenylaminocarbonyl]-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 4-(2,6-dimethylpyridin-3-yl)-3-methylaniline (D120) and 2,3-dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole (intermediate 3 in WO 95/06627) using a similar procedure to Example 4 as a pale yellow oil (44%). This was converted to its hydrochloride salt as an orange solid from acetone.

^{1}H NMR (free base) (250MHz, $CDCl_3$) δ (ppm): 7.72 (s, 1H), 7.38 (d, 1H), 7.32-7.25 (m, 2H), 7.07-7.00 (m, 2H), 6.74 (s, 1H), 6.43 (s, 1H), 4.09 (t, 2H), 3.84 (s, 3H), 3.20 (t, 2H), 3.15 (br s 4H), 2.65 (br s, 4H), 2.58 (s, 3H), 2.37 (s, 3H), 2.28 (s, 3H), 2.06 (s, 3H).

Example 128

5-Bromo-2,3-dihydro-1-[3-methyl-4-(thiazol-2-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 3-methyl-4-(thiazol-2-yl)aniline (D121) and 5-bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D15) using a similar procedure to Example 4 as a foam (64%). This was converted to its hydrochloride salt as a yellow solid from acetone.

^{1}H NMR (HCl salt) (400MHz, d^6DMSO) δ (ppm): 10.74 (br, 1H), 8.75 (s, 1H), 7.95 (m, 1H), 7.83 (s, 1H), 7.79 (m, 1H), 7.71 (d, 1H), 7.61 (s,1H), 7.59 (d, 1H), 7.45 (s, 1H), 4.20 (t, 2H), 3.45 (d, 2H), 3.35 (d, 2H), 3.25-3.05 (m, 6H), 2.84 (d, 3H), 2.56 (s, 3H).

Example 129

5-Chloro-2,3-dihydro-1-[3-methyl-4-(thiazol-2-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 3-methyl-4-(thiazol-2-yl)aniline (D121) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 4 as a beige foam (70%). This was converted to its hydrochloride salt as a yellow solid from acetone.

^{1}H NMR (HCl salt) (400MHz, d^6DMSO) δ (ppm): 10.77 (br, 1H), 8.79 (s, 1H), 7.93 (d, 1H), 7.82 (s, 1H), 7.79 (d, 1H), 7.71 (d, 1H), 7.61 (s,1H), 7.59 (d, 1H), 7.29 (s, 1H), 4.20 (t, 2H), 3.50 (d, 2H), 3.34 (d, 2H), 3.23-3.04 (m, 6H), 2.83 (d, 3H), 2.56 (s, 3H).

Example 130

2,3-Dihydro-5-methoxy-1-[3-methyl-4-(thiazol-2-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 3-methyl-4-(thiazol-2-yl)aniline (D121) and 2,3-dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole (intermediate 3

in WO 95/06627) using a similar procedure to Example 4 as a pale yellow oil (68%). This was converted to its hydrochloride salt as a yellow solid from acetone.

^{1}H NMR (HCl salt) (400MHz, d^{6}DMSO) δ (ppm): 10.56 (br, 1H), 8.64 (s, 1H), 7.94 (d, 1H), 7.77 (d, 1H), 7.69 (d, 1H), 7.65 (s,1H), 7.60 (s, 1H), 7.58 (d, 1H), 6.92 (s, 1H), 4.15 (t, 2H), 3.77 (s, 3H), 3.45 (br t, 4H), 3.14 (m, 4H), 2.96 (t, 2H), 2.81 (d, 3H), 2.55 (s, 3H).

Example 131

1-(5-Acetylnaphth-1-ylaminocarbonyl)-5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 5-acetylnaphth-1-ylamine (D124) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 4. This was converted to its hydrochloride salt as a buff coloured powder (60%).

^{1}H NMR (HCl salt) (250MHz, d^{6}DMSO) δ (ppm): 10.74 (s, 1H), 8.94 (s, 1H), 8.46 (d, 1H), 8.25 (d, 1H), 8.12 (d, 1H), 7.74 (s, 1H), 7.60 (m, 3H), 7.30 (s, 1H), 4.32 (br s, 2H), 3.45-2.90 (m, 10H), 2.75 (d, 6H).

Example 132

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[5-(pyrimidin-2-yloxy)naphth-1-ylaminocarbonyl]-1H-indole

The title compound was prepared from 5-(pyrimidin-2-yloxy)naphth-1-ylamine (D125) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 4. This was converted to its hydrochloride salt as a pale cream powder (61%).

^{1}H NMR (HCl salt) (250MHz, d^{6}DMSO) δ (ppm): 10.64 (s, 1H), 8.93 (s, 1H), 8.64 (d, 2H), 7.95 (d, 1H), 7.76 (s, 1H), 7.69-7.39 (m, 5H), 7.31 (m, 2H), 4.33 (br, 2H), 3.45 (m, 2H), 3.33-3.10 (m, 6H), 2.93 (t, 2H), 2.81 (s, 3H).

Example 133

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[5-(pyrimidin-5-yl)naphth-1-ylaminocarbonyl]-1H-indole

The title compound was prepared from 5-(pyrimidin-5-yl)naphth-1-yl isocyanate (D123) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 2 as a white foam (43%). This was converted to its hydrochloride salt as a white solid from acetone.

^{1}H NMR (HCl salt) (400MHz, d^{6}DMSO) δ (ppm): 10.48 (br, 1H), 9.33 (s, 1H), 8.98 (s, 1H), 8.95 (d, 1H), 8.20 (d, 1H), 7.76 (s, 1H), 7.57-7.67 (m, 6H), 7.31 (s, 1H), 4.39 (t, 2H), 3.43 (2H, obscured by water peak), 3.32 (d, 2H), 3.12-3.24 (m, 4H), 2.94 (t, 2H), 2.80 (d, 3H).

Example 134

2,3-Dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1-[5-(pyrimidin-5-yl)naphth-1-ylaminocarbonyl]-1H-indole

The title compound was prepared from 5-(pyrimidin-5-yl)naphth-1-yl isocyanate (D123) and 2,3-dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole (intermediate 3 in WO 95/06627) using a similar procedure to Example 2 as a white foam (50%). This was converted to its hydrochloride salt as a white solid from acetone.

^{1}H NMR (HCl salt) (400MHz, d^{6}DMSO) δ (ppm): 10.38 (br, 1H), 9.32 (s, 1H), 8.98 (s, 2H), 8.78 (s, 1H), 8.18 (d, 1H), 7.64 (t, 1H), 7.58 (m, 5H), 6.94 (s, 1H), 4.30 (t, 2H), 3.77 (s, 3H), 3.42 (4H, obscured by water peak), 3.12-3.23 (m, 4H), 2.89 (t, 2H), 2.78 (d, 3H).

Example 135

5-Chloro-1-(5-cyanonaphth-1-ylaminocarbonyl)-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 5-cyanonaphth-1-ylamine (D126) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 4. This was converted to its hydrochloride salt as a cream powder (81%).

^{1}H NMR (free base) (250MHz, $CDCl_3$) δ (ppm): 8.17 (d, 1H), 8.11 (d, 1H), 7.91 (d, 1H), 7.80 (m, 2H), 7.70 (t, 1H), 7.56 (t, 1H), 7.18 (s, 1H), 6.71 (s, 1H), 4.25 (t, 2H), 3.26 (t, 2H), 3.07 (br s, 4H), 2.59 (br s, 4H), 2.34 (s, 3H).

Example 136

5-Chloro-2,3-dihydro-1-[5-(5-methyl-1,2,4-oxadiazol-3-yl)naphth-1-ylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole

The title compound was prepared from 5-(5-methyl-1,2,4-oxadiazol-3-yl)naphth-1-ylamine (D130) and 5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole (D13) using a similar procedure to Example 4. This was converted to its hydrochloride salt as a buff coloured powder (84%).

^{1}H NMR (HCl salt) (250MHż, d^{6}DMSO) δ (ppm): 10.67 (s, 1H), 8.98 (s, 1H), 8.65 (d, 1H), 8.28 (d, 1H), 8.19 (d, 1H), 7.75-7.61 (m, 4H), 7.31 (s, 1H), 4.31 (t, 2H), 3.33-3.13 (m, 6H), 2.97 (t, 2H), 2.80 (s, 3H), 2.75 (s, 3H). 2H signal obscurred by H_2O signal.

Pharmacological Data

5-HT_{1A}, 5-HT_{1B} and 5-HT_{1D} Receptor Binding

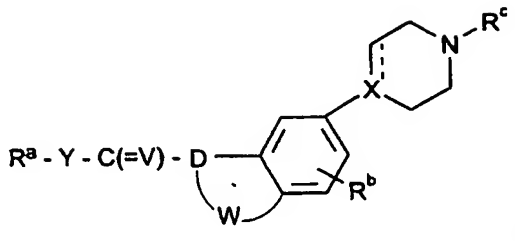
HEK 293 cells expressing 5-HT_{1A} receptors (4 x 10^7/ml) were homogenised in Tris buffer and stored in 1ml aliquots. CHO cells expressing 5-HT_{1B} receptors (4 x 10^7 cells/ml) were homogenised in Tris buffer and stored in 1.5 ml aliquots. CHO cells expressing 5-HT_{1D} receptors (0.563 x 10^8/ml) were homogenised in Tris buffer and stored in 1 ml aliquots.

0.4 ml of a cell suspension was incubated with [^{3}H]-5-HT (4nM) for 5-$HT_{1B/1D}$ receptors and [^{3}H]-8-OH DPAT (1nM) for 5-HT_{1A} receptors in Tris Mg HCl buffer (pH 7.7) and test drug, at 37°C for 45 minutes. Each test drug was tested at 10 concentrations (0.01 mM to 0.3 nM final concentration), with non-specific binding defined using 0.01 mM 5-HT. The total assay volume was 0.5 ml. Incubation was stopped by rapid filtration using a Packard Filtermate (filters pre-soaked in 0.3% polyethylenimine) and radioactivity measured by Topcount scintillation counting. pKi values were calculated from the IC_{50} generated by an iterative least squares curve fitting programme.

Examples 5, 9, 10, 15, 21, 24, 25, 27, 28, 43, 44, 45, 47, 48, 49, 50, 52, 53, 67, 68, 69, 70, 71, 72, 76, 78, 80, 81, 82, 83, 89, 97, 98 and 110 had pKi values >8.0 at 5-HT_{1A}, 5-HT_{1B} and 5-HT_{1D} receptors

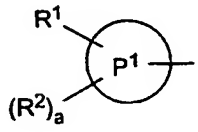
CLAIMS

1. A compound of formula (I) or a salt thereof:



(I)

in which R^a is a group of formula (i)



(i)

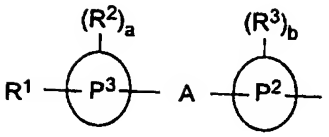
in which P^1 is phenyl, bicyclic aryl, a 5 to 7 membered heterocyclic ring containing 1 to 3 heteroatoms selected from oxygen, nitrogen and sulphur, or a bicyclic heterocyclic ring containing 1 to 3 heteroatoms selected from oxygen, nitrogen and sulphur;

R^1 is hydrogen, halogen, C_{1-6}alkyl, C_{3-6}cycloalkyl, COC_{1-6}alkyl, C_{1-6}alkoxy, hydroxy, hydroxyC_{1-6}alkyl, hydroxyC_{1-6}alkoxy, C_{1-6}alkoxyC_{1-6}alkoxy, acyl, nitro, trifluoromethyl, cyano, SR^9, SOR^9, SO_2R^9, $SO_2NR^{10}R^{11}$, CO_2R^{10}, $CONR^{10}R^{11}$, $CO_2NR^{10}R^{11}$, $CONR^{10}(CH_2)_cCO_2R^{11}$, $(CH_2)_cNR^{10}R^{11}$, $(CH_2)_cCONR^{10}R^{11}$, $(CH_2)_cNR^{10}COR^{11}$, $(CH_2)_cCO_2C_{1-6}$alkyl, $CO_2(CH_2)_cOR^{10}$, $NR^{10}R^{11}$, $NR^{10}CO_2R^{11}$, $NR^{10}CONR^{10}R^{11}$, $CR^{10}=NOR^{11}$, $NR^{10}COOR^{11}$ $CNR^{10}=NOR^{11}$, where R^{10} and R^{11} are independently hydrogen or C_{1-6}alkyl and c is 1 to 4

R^2 is hydrogen, halogen, C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkenyl, C_{1-6}alkoxy, C_{1-6}alkanoyl, aryl, acyloxy, hydroxy, nitro, trifluoromethyl, cyano, CO_2R^{10}, $CONR^{10}R^{11}$, $NR^{10}R^{11}$ where R^{10} and R^{11} are as defined for R^1;

a is 1, 2 or 3;

or R^a is a group of formula (ii)



(ii)

wherein P2 and P3 are independently phenyl, bicyclic aryl, a 5- to 7- membered heterocyclic ring containing 1 to 3 heteroatoms selected from oxygen, nitrogen and sulphur, or a bicyclic heterocyclic group containing 1 to 3 heteroatoms selected from oxygen, nitrogen or sulphur;

A is a bond or oxygen, S $(O)_m$ where m is 0 to 2, carbonyl, CH_2, $-CH_2CH_2-$, or NR^4 where R^4 is hydrogen or C_{1-6}alkyl;

R^1 is as defined above for formula (I) or R^1 is an optionally substituted 5 to 7-membered heterocyclic ring containing 1 to 3 heteroatoms selected from oxygen, nitrogen or sulphur;;

R^2 and R^3 are independently hydrogen, halogen, C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkenyl, C_{1-6}alkoxy, C_{1-6}alkanoyl, aryl, acyloxy, hydroxy, nitro, trifluoromethyl, cyano, CO_2R^{10}, $CONR^{10}R^{11}$, $NR^{10}R^{11}$ where R^{10} and R^{11} are as defined for R^1;

and a and b are independently 1, 2 or 3;

Y is -NH-, $-NR^5-$ where R^5 is C_{1-6}alkyl, or Y is $-CH_2-$ or -O-;

V is oxygen or sulphur;

D is nitrogen, carbon or a CH group; W is $(CR^{16}R^{17})_t$ where t is 2, 3 or 4 and R^{16} and R^{17} are independently hydrogen or C_{1-6}alkyl or W is $(CR^{16}R^{17})_u$-J where u is 0, 1, 2 or 3 and J is oxygen, sulphur, $CR^{16}=CR^{17}$, $CR^{16}=N$, $=CR^{16}O$, $=CR^{16}S$ or $=CR^{16}-NR^{17}$;

X is nitrogen or carbon;

R^b is hydrogen, halogen, hydroxy, C_{1-6}alkyl, trifluoromethyl, C_{1-6}alkoxy, C_{2-6}alkenyl, C_{3-7}cycloalkyl optionally substituted by C_{1-4}alkyl, or aryl;

R^c is hydrogen or C_{1-6}alkyl; and

—— is a single bond when X is nitrogen or a single or double bond when X is carbon.

2. A compound according to claim 1 in which R^1 is a halogen atom.

3. A compound according to claim 1 or 2 in which R^2 and/or R^3 are each hydrogen, halogen or a C_{1-6} alkyl group.

4. A compound according to any of the preceding claims in which P^1 and P^2 are phenyl, naphthyl or quinolinyl.

5. A compound according to any of the preceding claims in which Y is -NH- .

6. A compound according to any of the preceding claims in which D is nitrogen and W is a group of formula $-(CH_2)_2-$.

7. A compound according to any of the preceding claims in which R^b is a C_{1-6}alkoxy group.

8. A compound according to any of the preceding claims in which X is nitrogen.

9. A compound according to claim 1 which is:
1-[(4-bromo-3-methylphenyl)aminocarbonyl]-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole,
1-[(4-bromo-3-methylphenyl)aminocarbonyl]-2,3-dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole,
1-[(2,3-dichlorophenyl)aminocarbonyl]-2,3-dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole,
2,3-Dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole,
2,3-Dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1-[5-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole,
1-[2,3-Dichloro-4-(pyridin-4-yl)phenylaminocarbonyl]-2,3-dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole,
2,3-Dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1-(quinolin-5-ylaminocarbonyl)-1H-indole,
2,3-Dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole,

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)phenylaminocarbonyl]-1H-indole,

5-Bromo-1-[3-chloro-4-(pyridin-4-yl)phenylaminocarbonyl]-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole,

2,3-Dihydro-5-methyl-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole,

1-[3-Chloro-4-(pyridin-4-yl)phenylaminocarbonyl]-2,3-dihydro-5-methyl-6-(4-methylpiperazin-1-yl)-1H-indole,

2,3-Dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-5-vinyl-1H-indole,

2,3-Dihydro-5-ethyl-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole,

1-[3-Chloro-4-(pyridin-4-yl)phenylaminocarbonyl]-2,3-dihydro-5-ethyl-6-(4-methylpiperazin-1-yl)-1H-indole,

2,3-Dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-5-trifluoromethyl-1H-indole,

1-[3-Chloro-4-(pyridin-4-yl)phenylaminocarbonyl]-2,3-dihydro-6-(4-methylpiperazin-1-yl)-5-trifluoromethyl-1H-indole,

2,3-Dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylacetyl]-1H-indole,

2,3-Dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1-[5-(pyridin-4-yl)-naphth-1-ylacetyl]-1H-indole,

2,3-Dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylacetyl]-1H-indole

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylacetyl]-1H-indole,

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylacetyl]-1H-indole,

2,3-Dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylacetyl]-5-vinyl-1H-indole,

5-Bromo-2,3-dihydro-6-(1-methylpiperidin-4-yl)-1-[4-(pyridin-4-yl)naphth-1-ylamino-carbonyl]-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[5-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole,

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[5-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole,

2,3-Dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1-(quinolin-6-ylaminocarbonyl)-1H-indole,

2,3-Dihydro-1-[4-(*t*-butoxycarbonylamino)phenylaminocarbonyl]-5-chloro-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-(quinolin-6-ylaminocarbonyl)-1H-indole,

6-Bromo-7-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1,2,3,4-tetrahydroquinoline,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-(4-phenoxyphenylaminocarbonyl)-1H-indole

5-Chloro-2,3-dihydro-1-[4-(4-chlorophenoxy)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-(quinolin-6-ylaminocarbonyl)-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-(3-phenoxyphenylaminocarbonyl)-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyrimidin-2-yl)phenylamino-carbonyl]-1H-indole,

1-(3-Benzoylphenylaminocarbonyl)-5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole,

1-(4-Benzoylphenylaminocarbonyl)-5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-(2-methylquinolin-6-ylaminocarbonyl)-1H-indole,

5-Chloro-2,3-dihydro-1-[4-(fur-2-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(thien-2-yl)phenylaminocarbonyl]-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[5-(pyridin-2-yl)naphth-1-ylacetyl]-1H-indole,

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[5-(pyridin-4-yl)naphth-1-ylacetyl]-1H-indole,

5-Chloro-2,3-dihydro-1-[4-(1-methylpiperidin-4-yl)naphth-1-ylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-1-[4-(2-methyloxazol-4-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(2-methylpyridin-4-yl)phenylamino-carbonyl]-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(2-methylpyridin-4-yl)phenylaminocarbonyl]-1H-indole,

5-Chloro-2,3-dihydro-1-[4-(2,6-dimethylpyridin-4-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Bromo-2,3-dihydro-1-[4-(2,6-dimethylpyridin-4-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

2,3-Dihydro-1-[4-(2,6-dimethylpyridin-4-yl)phenylaminocarbonyl]-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-1-[4-(2,6-dimethylpyridin-3-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Bromo-2,3-dihydro-1-[4-(2,6-dimethylpyridin-3-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

2,3-Dihydro-1-[4-(2,6-Dimethylpyridin-3-yl)phenylaminocarbonyl]-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(5-methyl-1,2,4-oxadiazol-3-yl)phenylaminocarbonyl]-1H-indole,

5-Chloro-2,3-dihydro-1-[4-(3-methyl-1,2,4-oxadiazol-5-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[3-(pyrimidin-2-yloxy)phenylaminocarbonyl]-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-{4-[N-methyl-N-(pyrimidin-2-yl)amino]phenylaminocarbonyl}-1H-indole,

5-Bromo-2,3-dihydro-1-[4-(fur-2-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(thien-3-yl)phenylaminocarbonyl]-1H-indole,

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(thiazol-2-yl)phenylamino-carbonyl]-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(thiazol-2-yl)phenylamino-carbonyl]-1H-indole,

1-[4-(5-Acetylthien-2-yl)phenylaminocarbonyl]-5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole,

1-(5-Bromonaphth-1-ylacetyl)-5-chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-(8-phenylquinolin-5-ylaminocarbonyl)-1H-indole,

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-(8-phenylquinolin-5-ylaminocarbonyl)-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[2-(2-phenylethyl)quinolin-6-ylaminocarbonyl]-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[5-(1-methylpiperidin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole,

5-Bromo-2,3-dihydro-1-[4-(isoquinolin-4-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-1-[4-(isoquinolin-4-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(quinolin-3-yl)phenylaminocarbonyl]-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(quinolin-3-yl)phenylaminocarbonyl)]-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[(2-methyl-1,2,3,4-tetrahydroisoquinolin-7-yl)aminocarbonyl]-1H-indole,

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[(2-methyl-1,2,3,4-tetrahydroisoquinolin-7-yl)aminocarbonyl]-1H-indole,

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(quinolin-8-yl)phenylaminocarbonyl]-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(quinolin-8-yl)phenylaminocarbonyl]-1H-indole,

5-Chloro-2,3-Dihydro-1-[4-(imidazol-1-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridin-4-yl)phenylaminocarbonyl]-1H-indole,

2,3-Dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1-[(8-phenylquinolin-5-yl)aminocarbonyl]-1H-indole

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[(8-phenylquinolin-4-yl)aminocarbonyl]-1H-indole,

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[(8-phenylquinolin-4-yl)aminocarbonyl]-1H-indole,

2,3-Dihydro-5-methoxy-6-(4-methylpiperazin-1-yl)-1-[(8-phenylquinolin-4-yl)aminocarbonyl]-1H-indole,

5-Chloro-2,3-dihydro-1-[4-(2,6-dimethyl-pyridin-4-yl)-3-methylphenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-1-[3-methyl-4-(6-methylpyridin-2-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Bromo-2,3-dihydro-1-[3-methyl-4-(6-methylpyridin-2-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

2,3-Dihydro-5-methoxy-1-[3-methyl-4-(6-methylpyridin-2-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-1-[5-(6-methylpyridin-2-yl)naphth-1-ylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

2,3-Dihydro-5-methoxy-1-[5-(6-methylpyridin-2-yl)naphth-1-ylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-6-(4-ethylpiperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole,

5-Chloro-2,3-dihydro-6-(4-ethylpiperazin-1-yl)-1-[5-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole,

5-Chloro-2,3-dihydro-6-(piperazin-1-yl)-1-[4-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole hydrochloride,

5-Chloro-2,3-dihydro-6-(piperazin-1-yl)-1-[5-(pyridin-4-yl)naphth-1-ylaminocarbonyl]-1H-indole hydrochloride,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridazin-3-yl)phenylaminocarbonyl]-1H-indole,

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyridazin-3-yl)phenylaminocarbonyl]-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyrazin-2-yl)phenylaminocarbonyl]-1H-indole,

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[4-(pyrazin-2-yl)phenylaminocarbonyl]-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[(2-phenylpyridin-5-yl)aminocarbonyl]-1H-indole,

5-Bromo-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[(2-phenylpyridin-5-yl)aminocarbonyl]-1H-indole,

5-Chloro-2,3-dihydro-1-[4-(6-methylpyridazin-3-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Bromo-2,3-dihydro-1-[4-(6-methylpyridazin-3-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-l-yl)-1-[4-(pyridin-3-yl)phenylaminocarbonyl]-1H-indole,

5-Chloro-2,3-dihydro-1-[4-(5-methyloxazol-2-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

2,3-Dihydro-5-methoxy-1-[4-(5-methyloxazol-2-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Bromo-2,3-dihydro-1-[4-(5-methyloxazol-2-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-1-[4-(1-methylpyrazol-4-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Bromo-2,3-1-[4-(1-methylpyrazol-4-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-1-[4'-cyano-3'-methylbiphenyl-4-aminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Bromo-2,3-dihydro-1-[4'-cyano-3'-methylbiphenyl-4-aminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-1-[4-(2-methylpyridin-5-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Bromo-2,3-dihydro-1-[4-(2-methylpyridin-5-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-1-[5-(3-methyl-1,2,4-oxadiazol-5-yl)naphth-1-ylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

2,3-Dihydro-5-methoxy-1-[5-(3-methyl-1,2,4-oxadiazol-5-yl)naphth-1-ylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole.

5-Bromo-2,3-dihdyro-1-[5-(3-methyl-1,2,4-oxadiazol-5-yl)naphth-1-ylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-1-[5-(5-methyloxazol-2-yl)naphth-1-ylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

2,3-Dihydro-5-methoxy-1-[5-(5-methyloxazol-2-yl)naphth-1-ylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Bromo-2,3-dihydro-1-[3-methyl-4-(pyrimidin-2-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

2,3-Dihydro-5-methoxy-1-[3-methyl-4-(pyrimidin-2-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-6-(4-methylpiperazin-1-yl)-1-[3-methyl-4-(pyrimidin-2-yl)phenylaminocarbonyl]-1H-indole,

5-Bromo-2,3-dihydro-1-[3-methyl-4-(pyrimidin-5-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-1-[3-methyl-4-(pyrimidin-5-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

2,3-Dihydro-5-methoxy-1-[3-methyl-4-(pyrimidin-5-yl)phenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Bromo-2,3-dihydro-1-[4-(2,6-dimethylpyridin-4-yl)-3-methylphenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

2,3-Dihydro-5-methoxy-1-[4-(2,6-dimethylpyridin-4-yl)-3-methylphenylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Chloro-2,3-dihydro-1-[5-(2,6-dimethylpyridin-4-yl)naphth-1-ylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

5-Bromo-2,3-dihydro-1-[5-(2,6-dimethylpyridin-4-yl)naphth-1-ylaminocarbonyl]-6-(4-methylpiperazin-1-yl)-1H-indole,

2,3-Dihydro-1-[5-(2,6-dimethylpyridin-4-yl)naphth-1-ylaminocarbonyl]-5-methoxy-6-(4-methylpiperazin-1-yl)-1H-indole

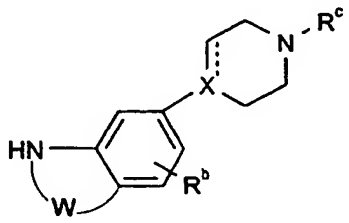
or a pharmaceutically acceptable salt thereof.

10. A process for the preparation of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof which comprises:

(a) where D is nitrogen and Y is NH , coupling a compound of formula (II):

R^a-NC(=V) (II)

in which R^a and V are as defined in formula (I) or a protected derivative thereof with a compound of formula (III).



(III)

in which W, X, R^b and R^c are as defined in formula (I), or a protected derivative thereof; or

(b) where D is nitrogen and Y is NH or NR^5 , reacting a compound of formula (IV)

R^a-NH_2 or R^a-NR^5H (IV)

in which R^a and R^5 are as defined in formula (I) with a compound of formula (III) together with an appropriate urea forming agent;

(c) where D is nitrogen, reacting a compound of formula (V)

$$R^a\text{-}Y\text{-}(C{=}O)\text{-}L^2 \qquad (V)$$

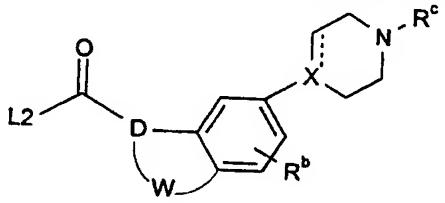
in which R^a is as defined in formula (I),

Y is $-CH_2-$ or -O- and L^2 is an appropriate leaving group, with a compound of formula (III)

(d) where D is carbon or CH, reacting a compound of formula (VI)

$$R^a\text{-}NH_2 \qquad (VI)$$

in which R^a is as defined in formula (I) with a compound of formula (VII)



(VII)

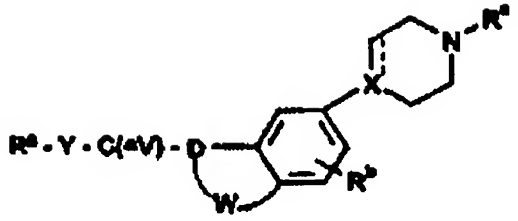
in which D is carbon or CH, W, X, R^b and R^c are as defined in formula (I) and L^2 is an appropriate leaving group

and optionally thereafter:

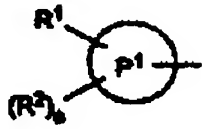
- removing any protecting groups,
- converting a compound of formula (I) into another compound of formula (I),
- forming a pharmaceutically acceptable salt.

11. A compound according to any of claims 1 to 9 for use in therapy.

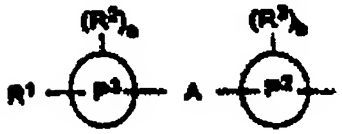
12. A pharmaceutical composition which comprises a compound according to any of claims 1 to 9 and a pharmaceutically acceptable carrier.



(I)



(I)



(II)